Granulomas

(Basics)

- **Def:** Compact or organized Collection of Histiocytes ± may be associated ± Accessory features as Caseation / Infilt. by other cells.

- Histiocytes are Tissue Macrophages that derived From Blood. Monocytes → Tissue → Histiocytes (2 Types)
  - Macrophage → (F) phagocytosis
  - APCs → (F) Ag presentation (as Langer. Giant cells)

In granuloma Histiocyte take 3 Types

1. **Histiocytes**
   - Rounded or Oval
   - Cytoplasm: Abundant Eosinophilic
   - Nucleus: large, pale, Oval, Vesicular

2. **Epithelioid Cells**
   (Epithelial or KC like = Tall cells)
   - Represent Activated Histiocyte ± 2ry Morphological changes.

3. **Multinucleated Giant Cells**
   [. Aggregation due to fusion of Many Histiocytes or Epithelioid Cells.

- They Have Surface RS → For Phagocytosis, Complement, Fc of IgG.

- Granuloma develops as an Immunological Response to non-degradable (undigestable) Ag ± Drugs, Infection, FB, etc..

Classification

(1) FB or Allergic
(2) Infectious or Non Infectious
(3) Pathological
   (i) Nodular
   (ii) Diffuse

Pathological Classification

Nodular

✓ A. Tuberculoid (epithelioid Hist. + Lymphocytes).

- TB
- Leprosy
- $
- Leishmania
- Rosacea (granulom.). (perifollicular)
- LMDF. (Perifollicular).

✓ B. Sarcoidal (Naked)

- Sarcoidosis
- Sarcoidal FB — Silica / Zirconium
- L-Nitidus.

✓ C. Palisading : —

Diffuse

(A) Suppurative

1. Deep fungal inf.
2. Atypical Mycobact.
3. Actinomycosis
4. Halogenoderma

(B) Foamy.

1. Xanthoma
2. XG
3. Leprosy (HL)
4. Reticulohistiocytoma.

Multinucleated Giant Cells

- Formed by fusion of Multiple < Epithelioid Cells (or) Macrophages (Histiocytes)
- Types:
  - → Langhan Giant Cells: Nuclei arranged orderly at Periphery (Horse shoe)
  - → FB Giant Cells: Nuclei arranged Randomly in the Cytoplasm
- Function: ⊕ Trapping disposable unnecessary mononuclear Cells Entering area of Inflamm.

Multinucleated Giant Cells

(Epithelial)

1. Epidermal Giant Cells : HSV
2. Langhans multinuc. Giant Cells
3. F.B Giant Cells
4. Touton Giant Cells - Xanthomas (Sp. JAG)
5. Melanocytic Giant Cell - (Eg. Mc. Nevi & melanoma)
6. Endothelial Giant Cells (CMV)
7. Reed-Sternberg cells (see Lymphoma)

Classification of Granuloma

(A) Aetiological Classification

- Granuloma
  - Foreign-body granuloma
    - Exogenous: Oil, starch, silicon, etc.
    - Endogenous: Keratin, sebum, urates
    - → Foreign-body G. shows: (3)
      - ⊕ Histiocytes
      - Few or no epithelioid cells
      - Giant cells (large with irregular arrangement of the nuclei) → FB Giant Cells.
  - Allergic granuloma
    - Infectious: TB, leprosy, syphilis, deep fungi
    - Non-Infectious: Sarcoidosis, Palisading Gran.
    - → Allergic G. shows: (2)
      - Epithelioid cells
      - Multinucleated giant cells (Langhans) with small horse-shoe nuclei.

- Function of Granuloma: it is considered as Type IV Hypersensitivity reaction to Isolate or Eliminate An. Ag.

· Classificat⁻ of MYCobact.

Slow growers (2-3 ws)

(i) **photoChromogens**: تتلون صبغة صفرا مع التعرض للضوء

- M. Marinum
- M. Kansasii

(ii) **SCotoChromogens**: تتلون صبغة صفراء بدون التعرض للضوء

- M. SCrofulaCeum → L-N

(iii) **Non-Chromogens**:

- → M. TB & Bovis, BCG
- → MAIC, ulCerans, Hemophilum

Rapid growers (3-5 ds)

7 ds

- M. Chelonae, Abscesus, fortuitum

Non-Cultured

- M. Leprae

Mycobacterial Infection

تقنية سريعة

(Myco = Produce mold like Thin growths on liquid Media)

- Group of bacteria ch By.
  - Aerobic, Intracellular
  - Slender (Curved Rods)
  - Non motile
  - Non Spore forming
  - Resist staining (d.t Lipid rich cell Wall) & Lysosomes.
  - Resist decolorization by acid & alcohol (after staining) $\xrightarrow{\text{So called}}$ Acid fast/Alcohol fast.

- Structure. have cell wall the Contain: Large amount of lipids as:
  - Mycolic acids.
  - Fatty acids.
  - other lipids

↓

1. Ability to retain "Carbol Fuchsin dye" after washing by acids & Alcohol

So Called

Acid fast & Alcohol Fast $\Rightarrow$ Resist decolorization by $\begin{cases}\text{acid}\\ \text{Alcohol}\end{cases}$

2. Resist Lysosomal Attack.

- Types:

A
- Typical → TB & Leprosy
- Atypical → inf. other than TB or Leprosy

B According to the Culture
1. Slow growers (2-3 w)
2. Rapid " (3-5 d)
3. Non-Cultured.

NB

Other Alcohol & acid fast:
- Nocardia
- Cryptosporidium.

NB

- TB: Stain
  - (i). Z.N: specific, Not Sensitive (Need 10-00 organism/ml)
  - (ii) Auramine Rhodamine More Sensitive

TB of the Skin

- Rare dis. caused by Any Cobact. TB (Primary)
- Represent [1% of Extra P.Lm. TB.
  4% of all Cases of TB.
- Predisposing factors (↓↓ CMI):
  - Cytotoxics.
  - Cs.
  - Lymphoma.
  - Malnutrit°.
  - HIV ;)
- Risk is 500 Times Higher than in NL People
- Mainly d.t. M. Avium & M. Kansasii
- Less common: M. TB
- on vet < M. Avium: occurs Late when there is marked ↓ CD4.
  M. TB: occurs Early.

- 1ry TB Complex:

Primary Sites of TB±:

1. Lung (Inhalat°)
2. Tonsils (لوزتين)
3. Skin (if no Calot° or Haem. or Lymph. Spread) = (Fom Skin → Skin)
4. Intestine. (لو شرب لبن ملوث) (M. Bovis)

- M. TB Complex (3 strains are pathogenic to Human)
  1. M.TB (95% of TB inf. in Human)
  2. M. Bovis (Transmitted from Cattle to Human via milk)
  3. BCG

Cutaneous TB

- There are 2 forms of TB Inf. of the Skin:
(Tuberculoderma s):

Ⓐ - True Tuberculoderma : Actual Invasion by Bacilli

Ⓑ - Tuberculid : Allergic Reaction to Bacilli or their products.

True Tuberculoderma:

- Can be classified acc. to:

1. Mode of Inoculation
2. Host Immunity.

① Exogenous:
- TB chancre. (TBC)
- TVC.

② Endogenous:

(i) Autoinoculation: TCo

(ii) Contiguous spread: SF

(iii) Hematogenous / Lymphatic:
- Lv
- Acute miliary TB.
- TB Gumma. : child, malnourish, Single or multiple, Nodul. → ulcerat & Fistula

- Most Common Types:
  - TVC
  - Lv
  - SF

(دائيوي)

- The Most Common Types in: (i) Children: SF
(ii) Adults:

Acc. to host immunity:

- Good immunity (++CMI, ↑ Lymphocy. ↓ Caseat & Bacilli)
  1. Lv
  2. TVC
  3. Tuberculida.

③ (Poor Bacillary TB)

- Poor immunity (Hematogenous TB) ④ (adult)
  - SF
  - Tco
  - TB Gumma
  - Acute miliary

اسعط كلمتين باختصار
عن كل نوع

TB. Chancre (1ry Cut. Complex —Correspond To→ Gohn focus)

Inoculat: . Face . LL . mm
↓ 2-4 ws
Cut. lesion
↓ 3-8 ws
L.N

- Rare cut TB of skin d.t direct exogenous inoculation of organism into the skin or mm of an individual who has Neither: Natural Nor artificially Acq. Immunity (BCG)

Direct inoculation
↓ 2-4 ws
Skin lesion + L.N

asympt, red-brown papule or nodule → ulceration (Painless, Bluish Margin, Necrotic & G.T of Floor, Indurated Base)

[illegible]
Painless & Indurated ← [illegible]

↓

Fate

If good immunity
↓ Early Healing (1-3ms)
T cells destroy the bacilli ē granuloma formation —3-12 ms→ Healing by scar. + Calcified regional L.N

- Tuberculin: . Early, -ve
  . Later, +ve

If bad immunity:
↓
- The organism remains Latent & Later reactivate &
- May Evolve into:
  - LV
  - TVC
  - SF
  - military TB.

TB Verrucosa Cutis = Warty TB. (Anatomist / Butchers Wart) (Verruca necrogenica)

- Def: TB inf. of skin (d-t) Exogenous inoculation of the organism in patients who had (Eg. Imm.) either (Natural / Artificial) (either d-t previous inf. or Immunization)
- Site: Hands (but any site ± affected)
- Clp: - Hyperkeratotic, Warty, Verrucous plaque
  - ± Peripheral extension & Central Fissuring, Crusting & Scarring .. No L.N .. (±) Spont. Healing & Scar
- HP: (i) Hyperkeratosis (ii) PEH

(ii) Dermal:
- Abscesses
- Granuloma: Giant Cells, No Bacilli

TB Scrofuloderma (SF) (Most common Type in Children)

- TB infection of the skin d-t contiguous endogenous Extension from an underlying infected Tuberculous:
  - LN (Commenst, usually Cervical ± axillary) → طفرة بشرية M. Bovis → Tonsillar ± oral lesion → Cervical aden. → Cold Abscess → fistula to skin.
  - Bone
  - Joint or
  - Epididymis. (Post-Scrotal d(ter)

- Clp: the Most Common sites are: Inf. Neck & Parotid area. Bluish SC Nodule → Accumulate Pus & Exudate (Cold Abscess) → ulcerate (Liquid) & Sinus formation → Healing → Puckered or Hypertrophic Scar.
- DD of Axillary lesions: H. Suppurativa

TB Gumma (Metastatic TB abscess): Variant of scrofuloderma

that occurs d-t Hematogenous spread of Mycobacteria to skin

Clp: Single or Multiple Painless S.C (Abscesses) → break down → Fistulas & ulcers (as in SF). Uncommon, except: Malnourished children at Extremities.

حول فتحات الجسم (3)

Tuberculosis Cutis orificialis (TCO) → (ulcer)

· TB Inf. of skin & MM adjoining the body orifices:

d.t. Autoinoculation:
- · Pulmonary TB —autoinoculation→ orificial TB
- · Intestinal TB → Perianal TB
- · Genitourinary TB → Penile & Vulvar

· Orificial TB: (commonest): Tongues usually affected (Tip & Sides)
& may be Tooth sockets after Extraction

Oral Ulcer
· Very painful
&
Very resist

· lesion: Red Papule → Multiple painful soft punched out shallow
Very painful ulcers (e.g.) (Not tendency for spont. Healing).

· NB: Pts. usually < Elderly.
have severe Inf. organ disease & appearance
of TCO → Poor prognosis.

احفظ لوپين

Lupus Vulgaris (LV) (Clinical)

· The 2nd Most Common Type of Cut. TB, starting in Childhood & progress. & occur in pts ē very good imm. → "Tuberculin Test (++Ve)

Epidemiology
Age 20-40.
Sex:
M > F
(3 : 1)
(Sacoid)

· It occur as a result of:

[1] Exogenous ... site of previous TB chancre
(the organism may remain latent & then
Reactivated → LV).

[2] Endogenous (+++) ← Haematogenous
Lymphatic: from (mucosa) → < Nose / Throat
direct: from underlying Joint or gland.

[3] Obscure Route ??

· Clp · · Origin Either on Top of NL Skin (more common) or on Top of ← BCG SF TVC

· Site: ← Commonly: Neck & face sp. ← Nose, cheeks, Ear lobes
← Less common: buttocks & limbs. (in Tropics) Common.

· What is LV Lesion?

Single plaque composed of Papules & Nodules:

-- Soft (Apple-jelly like).

· Reddish - brown in color

· Diascopy test → « apple jelly color » [yellow brown Spots]

The plaque [Periphery: → Serpigenous Extension
Center: Scarring clear ← thin, contractile, unhealthy

(new lesion start appears on areas of atrophy).

· clinical varieties:

1. Plaque forms: Psoriasiform ē No ulcerate No Scarring.
2. Nodular (Tumidus): large soft Tms on ear lobes with No ulcerate Ner Scarring
3. Vegetative: Necrosis ulcerate with minimal Scarring
4. Ulcerative & Mutilating: marked ulcerate, Scarring & Crust format → Deep tissue & Cartilage invasion → Contracture & deformities.
5. Mucosal.

(Lupus Vorax)

- Complications of LV:

destruct^n
Reactivat^n
Mg Trasformat^n

1. Scarring & destruction of < Cartilage e.g. Ear & Nose (→ Lupus Vorax) / MM — Nose, oral } microstomia; Eye → Ectropion.

2. Reactivation after apparent healing (unhealthy scar).

3. Mg Transformation: SCC (++) & BCC (+)

(Pathology) → Tuberculoid Granuloma: (upper dermal):

- Epithelioid cells
- Langhans Giant cells
- (dense) mononuclear (Lymphocytes & monocytes) infilt. ē slight (or) Absent
  - (±) Caseation (minimal)
  - TB bacilli (-ve) (Absent).
- Epid. Changes as: Atrophy, Hypertrophy & Hyperplasia, ulcerat^n.

- DD of Tuberculoid Granuloma

- TB
- TT
- Sarcoidosis

Sarcoid.

- LMDF
- Granulomatous Rosacea
- Atypical Mycobact.
- $

- FB Granuloma
- Deep fungal Inf.

PLEVA like

Acute - Miliary TB < Immuno Compromised. Hematogenous.

- Miliary, sized, red-Blue papules, Vesicles, Pustules, Hg^ic lesions → Crustat^n → white scar ē Brownish rim (PLEVA like).

Tuberculids (Eruptive TB)

· Def: Cutaneous Eruption Caused by Hypersensitivity react^ to TB bacilli or their products (Ag.) affecting patient ↓ Good CMI d.t Hematogenous dissemination of Ag

· NB: patients with Tuber culids are in relatively good health & show:

1. +ve Tuberculin Test. (Good CMI).
2. Evidence of TB focus (usually inactive) Elsewhere.
3. -ve staining & Culture for Pathogenic Myco-bacteria in the lesions. (but PCR +ve)
4. Skin lesions Heal either Spontaneously or ^ ## & TB
5. Tuberculoid Granuloma except Caseation

· Etiology: (1) Old theory: Hypersensitivity react^ to remote site of TB inf. (against bact. Ags)

(2) Recent: Hematogenous dissemination^ of Bacilli to skin → reflects destruct^ by Good CMI (PCR Detect TB DNA in papular & Nodular Types only)

· Types: 1. Lichen Scrofulosorum (micropapular)
2. papulonecrotic Tuberculid (Commonest type) (papular)
3. Erythema Induratum of Bazin's (Nodular)

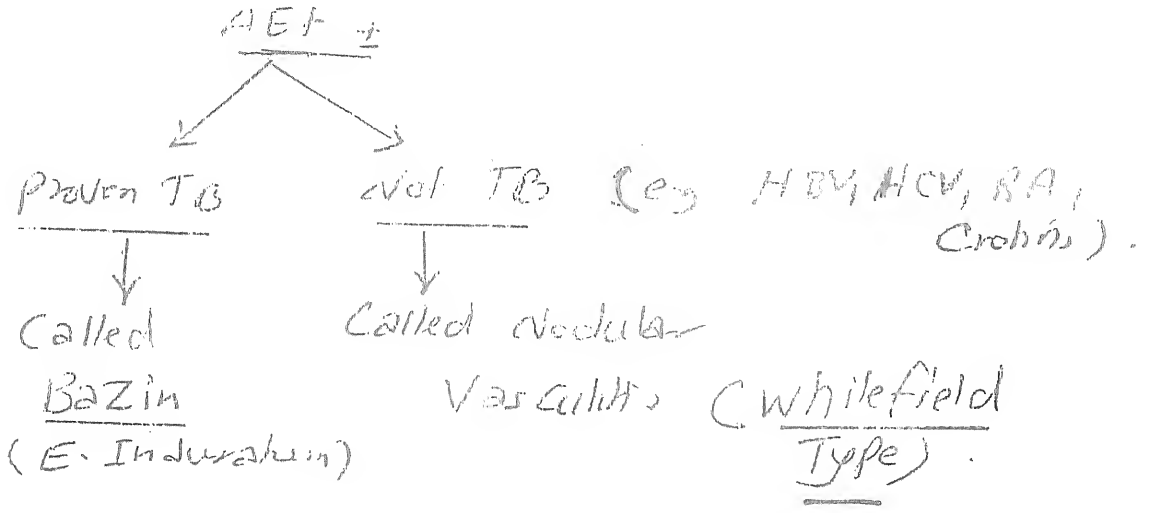
Children & young Adult

1. Lichen Scrofulosorum
   - Bilat, Symm., Asympt., grouped, perifollicular, Lichenoid Papules ē Exacerbat^ & Remission → No Scars.
   - at Trunk
   - Hp: perifollicular Tuberculoid Granuloma – No Bacilli, No Caseation
   - DD: All follicular disorders
     - Sarcoid, S, Id. react^.
     - LP
     - L-Nitidus.
     - K-pilaris

2. papulonecrotic Tuberculid (PLEVA like)
   - Asympt., Bilat., Symm.
   - Dusky red, papules or papulopustules ē Central Necrosis → "pox like scars"
   - at Extensor Extremities.
   - Hp: Tuberculoid Granuloma
   - Lev. +
   - DD: PLEVA & prurigo

3. Erythema Induratum (Bazin's dis) [Nodular Vasculitis]

Def: lobular Panniculitis (e) Vasculitis.



· Clp: · ♀, obese, 40 ys.
· Winter → Exacerbat
· Erythem- Violaceous, SC Nodules & plaques at (Calve, Thigh, Buttock)
→ Involution or break down with → Irregular deep ulcers with undermined blue borders → "Atrophic (Hyperpigmented Scars".

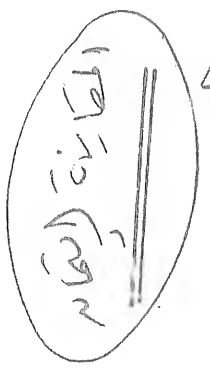
الالتهاب الشحمي

· Path. · Panniculitis (Mostly Lobular) + Vasculitis

EN
· Septal Panniculitis without vasculitis
· prefibral
· No ulcerat^
· Et- TB, but HSV
· Ht: Antimflam

· DD: EN, PAN, lupus panniculitis, S.C panniculitis Like TCL & perniosis.

(Tt) < Anti TB / KI

NB


· EN (Mostly septal panniculitis & vasculitis)
· LMDF
· Lichenoid tuberculid
· Rosacea (granulomatous)
→ No longer considered as Tuberculids.

* BCG inoculation (اللقاح)

Rx of Tuberculids: (1) Anti TB drugs (الأدوية المضادة للسل)
(2) other antibiotic.
(3) plenty rest & other supportive measures.

Diagnosis of TB cutis

Absolute criteria : (3) [c]

1. +ve culture on Lowenstein-Jensen's medium of M. tuberculosis from the lesion.
2. Guinea pig inoculation.
3. PCR

Relative "unreliable" criteria : (6)

1. Clinical history & signs.
2. Presence of active proven TB focus elsewhere in the body.
3. Presence of acid-fast bacilli in the lesion itself.
4. Histopathology.
5. +ve reaction to tuberculin.
6. Effect of specific therapy.

Criteria for diagnosis of tuberculids :

1. +ve tuberculin test.
2. Evidence of TB elsewhere.
3. Tuberculoid granuloma on histological examination.
4. Good response to anti-tuberculous drugs.

NB . TB investigations :

1. AFB Staining & Culture
2. Guinea Pig inoculation
3. Histopathology (HP)
4. Tuberculin test
5. PCR (Tissue) →
6. Interferon γ Release Assay (IGRA) (Blood) → (FDA-2005)

, Measurement of T cell IFN-γ response to Ags that are Highly-specific for M.TB & Absent from BCG & M. avium.

2 Types of this test:

(QFT-GIT) → (i) QuantiFERON-TB Gold In Tube test:

Pt. Serum + 3 Ags → ELISA Assessment of IFN-γ level

(ii) T. SPOT-TB : 2 Ags + pt. Serum → Measuring The Number of IFNγ producing Cells.

- NB → QFT-GIT : IFNγ مستوى يقيس
  T. SPOT. TB : IFNγ producing يقيس T-cells .

TGRA

(A) · Advantage :

(i). Sensitive > Tuberculin ((-Ve ē < BCG / M. Avium))

(ii). Single visit test (Tuberculosis تشخيص بزيارة واحدة)

(B). disadv.

(i). Expensive

(ii). difficult

(iii). Lack of prospective studies.

(iv) may be -ve in Early Inf. or False -ve ē M. avium

· Tuberculin Skin Test (Tuberculin Mantoux Test).

· 5 units (0.1ml) of PPD $\frac{2-3}{d}$ → (Induration) (Not Erythema)

> 10 mm in diameter → +ve Test. (doesn't differentiate bet. past & present Inf.)

· Interpretation

(1). The test is not Specific; False +ve result: May occur ē BCG vaccination & MAIC Inf.

(2) False -ve results.

- Immunosuppressives
- Multibacillary Types of TB Inf.
- Sarcoidosis (سرطان)
- Lymphoma
- Very Early Inf. (< 3-8 wks)

TABLE 10-2 FIRST-LINE ANTITUBERCULOUS AGENTS AND MAJOR SIDE EFFECTS

Drug	Side Effect	Special Comment
Isoniazid	Peripheral neuritis	From pyridoxine deficiency (+ Pyridoxin 10mg/d)
	Hepatitis	Occurs with 1–2% increased risk with age >35
Rifampin	Hepatitis	
	Orange stain of secretions	May permanently stain contact lenses
Pyrazinamide	Hyperuricemia, Hepatitis	May precipitate gout
Ethambutol	Optic neuritis	Avoid in children under age 13
Streptomycin	Vestibular toxicity	Most common in elderly
	Hearing impairment	

Visual Acuity & green color perception Testing.

(3)

(H) Cut. TB

"كلهم تاخدوا على معدة فاضية جرعة واحدة يوميا"

. Drugs used:

. Isoniazid (INH): (أهم واحد) (C)

- 300 mg/d for adults
- 6 mg/Kg/d for Children

. Rifampacine: (C)

- Children: 20 mg/Kg/d.
- Adult < 50 Kg: 450 mg/d
- " > 50 Kg: 600 mg/d.

. Pyrazinamide: (C)

- < 50 Kg → 1.5 g/d
- 50-75 Kg → 2 g/d
- > 75 Kg: → 2.5 g/d.

. Ethambutol: 15 mg/Kg ✓ (C)

. Streptomycin: 0.75 gm IM/d.

. Paraminosaliqylic acid: 10 gm/d.

Pregnancy TB

- 500 times ↑ risk in early
- Rifampicin not given c̄ protease inhibitor.

Vit D2 (Calciferol)

150000 IU for 5 ds → ++ Fibroblast → strangling TB.

Bedaquiline (Sirturo)®

- ATP synthase of MTB

أحدث واحد وافق عليه FDA (2012)

. Regimen . 4 X2 . 2 X4 (٦ شهور كلها)

⊙ Intensive = Initial phase

. 4 drugs for 2 ms
- INH
- Rifamp.
- Pyrizinamide.
- + either Ethambutol or Streptomycin

(Initial Empiric) بنبدأ مباشرة اول ما نشخص كحالة. وبعدين تأكد ان الميكروب بيستجيب لهم عن طريق الزرعة. بنشيل واحد من ٢ فيبقى تنين

Continuation phase

. (2) drugs for (4) months. (INH & Rifamp.)

. لو حصل لل Resistant Hep. لل INH . pyrizin. . Ethamb. هانحط مكانه

يعمل كله ٦ شهور

DOT (Directly observed therapy)

نضمن انه خد العلاج بانتظام لما يطلب علاج لمدة ٦ شهور ممكن ينسى كام مرة ٢-٣ مرات في الاسبوع

- DOT → بيبقى قدام الدكتور
- Daily → لوحده في البيت

A Typical Mycobacteriosis (non Tuberculous Mycobact)
(Environmental Mycobact).

. Why Called Atypical Mycobact ??

. Not as TB & M. leprae because:

1. present Freely in the environment (ubiquitous) as: Water, Soil & animals.
2. Not always pathogenic (low virulence)
3. Not transmitted From Person to persons (but From environment by inhalation or Skin trauma) ← So better Called [enviromental Mycobact]
4. predisposing conditions must be present to produce inf. e.g obst. pulm. dis, Trauma, Immuno-supp. (HIV)
5. Poor Response To Anti-TB drugs.

. A typical Mycobact. include:

. 2 Lung ← MAIC, Kansasii → (Immunocomp)
. 3 Skin ← Marinum, ulcerans, Chelonae/Abscessus → (" Competent)

also called M.A. Complex (MAC) → . M. Avium-inter Cellulare
M. Kansasii
] • Primarily Cause Lung dis. similar To TB

M. Marinum (Commonest Type)
M. ulcerans
M. chelonae / abscessus. gp.
] → Cause Skin inf

* Cut. infection usually in form of ulcerated Nodule.
(Indolent ulcer, Nodule or plaque) : • توقعها لو لقيت

(اتكلم عن كل واحد بالتفصيل)

. MAC

.. Commonest Non TB Mycobact. infection in HIV patients (occurs Late when there is marked ↓ CD4+ while TB less frequent & occur Early)

General manif. + Pulmonary affection + Skin
[. Fever . Wt loss
[. Fatigue . L.N
(1) Purulent Leg ulcers
(2) papulo-pustules
(3) S.C Nodules

M. Kansasii

- 2nd Most Common Type
- usually affects patients ē HIV or COPD
- C/P:
  1. General Manifs.
  2. Pulmonary: TB like
  3. Cut. (i) Sporotrichoid Nodules
     (ii) Verrucous "
     (iii) Papulopustules
     (iv) Cellulitis.

M. Marinum

→ Fish-tank granuloma. (حمامات)

M. ulcerans

→ **Buruli ulcer:**

غانا . أوغندا . الكونغو . سيبيريا . أمريكا الجنوبية . — وسط أفريقيا

- Solitary Painless Sometimes Itchy Nodule (1-2 cm) after an (IP: 1-3 ms)
- 1-2 ms → Break down → Rapidly spreading Shallow ulcer That may Involve up to 15% Body & ± [illegible]: BVs, Nerves
- Healing ē fibrosis → Joint Contracture.

M. fortuitum Complex

3 Types:
- Chelonae (Abscessus)
- Fortuitum, Smegmatis

Commonest: sporotrichoid S.C Nodules on distal Limbs

- Present in Tap water, soil, dust.
- may → Lung → pneumonia
  - Eye → keratitis, Endocarditis (Heart)
  - Joint
  - Skin:
    - ImmunoCompetent: localized Abscess Complicating Traumatic injury (wound, Abrasion, Catheter)
    - ImmunoCompromised: No Hx of Trauma (injury), disseminated Nodules, L.N, +ve Blood Culture.

Treatment of cutaneous non-tuberculous mycobacterial infection

Micro organism	First Line	Other considerations
M chelonae	Clarithromycin + ciprofloxacin/doxycycline	Surgical debridement Dual antimicrobial therapy
M fortuitum	Amikacin + ciprofloxacin/doxycycline	Surgical debridement Dual antimicrobial therapy
M absessus	Clarithromycin + amikacin/cefoxitin	Surgical debridement/excision
M marinum (٣-٤ شهور)	Ethambutol + rifampicin or doxycyc.	Surgical debridement
M avium-intracellulare (سنتين)	Ethambutol + clarithromycin + rifampicin	Surgical excision
M. Kansasii (9-18 ms)	3-4 drugs For 18 ms.	
M. ulcerans	Antibiotics Not effective	Surgical Excision → graft

Fish Tank Granuloma

سمك استكام

البحر ده اتكلم عليه ؟ → (Swimming pool Granuloma)

Def: Cut. skin inf. caused by Atypical Mycobact. (M. Marinum) manifested as (localized granuloma) or Sporotrichoid Lymphangitis.

Aet: → M. Marinum: Ch. By

- Non motile, Atypical AFB
- Grows in 2-3 wks on Lowenstein - Jensen Medium (at 32°C)
- They Can Produce:
  - Yellow pigment on Exposure to light (photo-Chromogen → Runyon group 1)
  - Urease & Catalase

Route of Inf.: • Exposure of breaked or Abraded Skin

[Any Aquatic env. + Skin trauma]

To M. Marinum (M) may be present in:

1. Aquarium (حمام مائي)
2. Salt water
3. Marine animals (Fish & Turtles)
4. Swimming Pools (rare): → استخدام الكلور

أي حد بيتعامل مع مياه أو أسماك

- So Risky patient are:

عشان كده → 1. Fishermen
2. Fish Processing workers [اللي بيتعاملوا مع السمك]
3. Salt water Aquarium Personnel
4. Immunocompromised.

C/P : (IP): 2-3 ws

. The organism infect the skin through minor abrasions during dealing with infected water.

. lesson: . Papule or Nodule at site of Trauma (Commonest is Hand & [Arabic handwriting]).

↓

Supparat^n & ulcerat^n

±

- Sporotrichoid Pattern
- Deeper: SCT & Bone affect^n

. Inv: (1) Radiography: XR, CT, MRI ⟹ to detect deeper Invasion.

(2). Biopsy: → Supparative granuloma with AFB & No Caseat^n.

"مهم"

(Sporotrichoid diseases)
(Sporotrichoid lymphocut. Inf)

. Def. Inf. Ch By appearance of S.C. Nodules along dermal & lymphatic v.

. C/P early lesion start as Nodule (±ulcerat^n) → distally at UL (Fingers or wrist) → irregular, linear Rough Spread along forearm.

(Et)

. Sporotrichosis
. Atypical Mycobact. (Marinum)
. Leishmaniasis.

. Treatment: For 3-4 ms (or 1-2 m, after disapp. of S&S)
. deeper inf. → ± up to 2 ys.

Tyre. Clarithromycin + Ethambutol
. others: Doxy - Mino, Fluroquinolones, Septrin
. Resistant to: INH; Pyrizinamide & PAS.

(Recently) lenalidomide (Thalidomide derivative act by Immunomodulat^n).

. Staph & Strept, Nocardia, Tularemia
. L.L & LV.
. Fungal Histoplasmosis, Cryptococcosis
. Non Infectious: Lymphoma / LCH / in-Transit Metastasis

Sarcoidosis

Def → Multi system granulomatous disorder ⓦ (Ch. By)
presence of wide spread, Non Caseating
Epitheloid cell granulomas in ≥ 1 system.

. AET → unknown but may be d.t:

Antigenic insult in Genetically predisposed → ↑ Incid of HLA: . B8,7 . DR3 . DRB1

Immunological React → Granulomatous React.

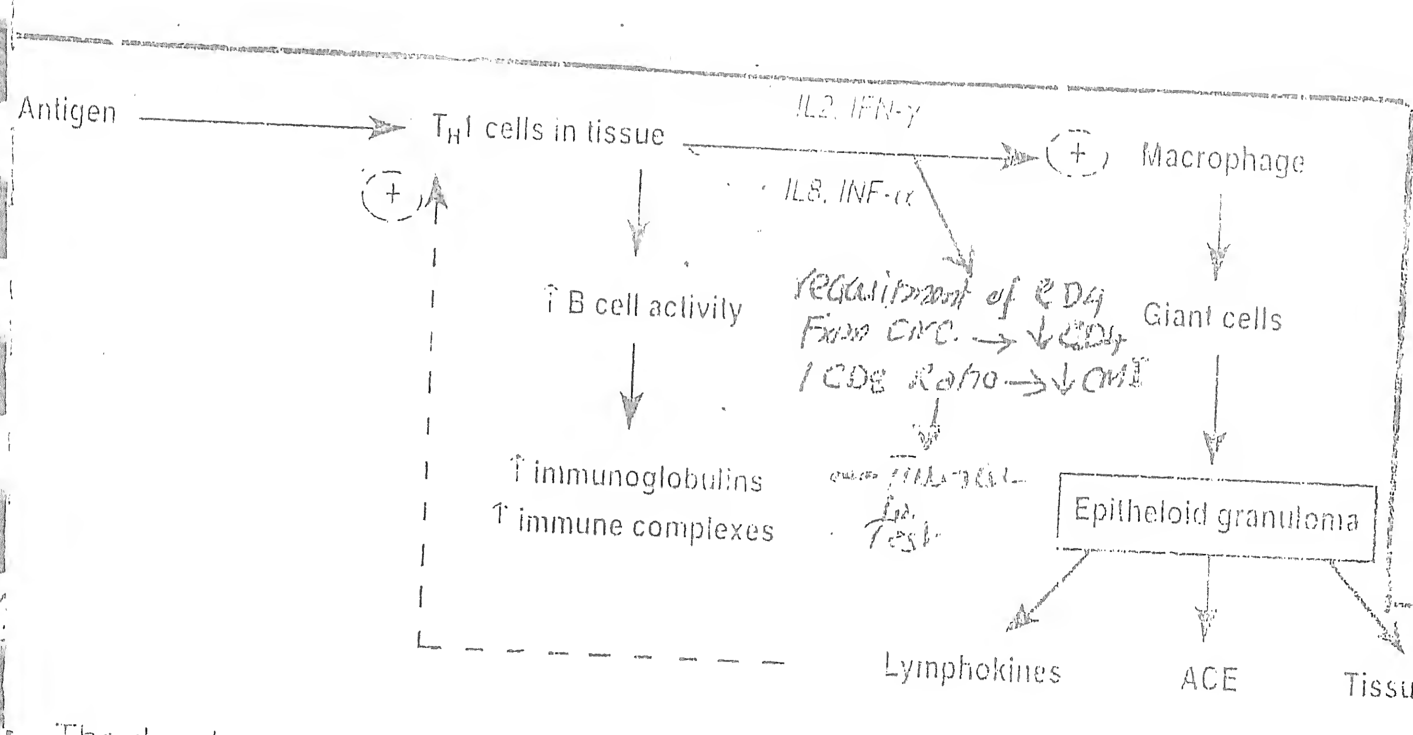
ⓦ may be:

1. Infective
   - Mycobact. (M (ParaTB, Avium))
   - (HSV-8)
   - Propionibacteria
   - BCG vaccin
2. Chemical
   - Beryllium
   - Talc
   - Pine pollen
   - Clay
3. Genetic
4. environmental
5. Immunologic ← (↑ HI, impaired CMI)
   ↓
   Sarcoidosis

Immunological Abnormalities

↑ Humoral Hypersensitivity
- ↑ Serum Igs.
- ↑ Immune complexes → EN, Poly arthritis, Uveitis.

(↓↓) Impaired CMI
. evident by
- (a) weak Tuberculin / Trichophytin skin test
- (b) failed DNCB to induce contact sensit.



Ag → Th pass to site of dis → leaving behind (in serum) Anergic suppressor T cells

So < tissue: Th/Ts = 5; Blood: 0.8 (N = 1.8)

d.t ↑ Suppressor.

The development of non-casealing granulomas is due to local presentation of an antigen by macrophages to T_H1 cells.

Ass. dis ⓦ Sarcoidosis
- a). Thyrotoxicosis
- b). Cryptococcosis
- c). Vasculitis
- d). NH Lymphoma
- e). Cancer lung
- f). GN

- Epidemiology:
  - Age: 20 - 40 y.
  - Sex: F : M = 1 : 2
    (M > F)

C/P

- Any organ can be affected by Sarcoidosis
  Except the Suprarenal gland.
- Usually start at the Lung (or) L.N of the Chest
  & then involve other organs:
  - Lung : 90 %
  - Liver : 30 - 40 %
  - Skin : 20 - 30 %
  - Eye : 20 - 30 %
  - Musculoskeletal : 2 - 35 %

Not.
- Heart.
- Parotid.
- Kidney.
- Nervous

- So C/P of Sarcoidosis is

Systemic → See above

Cut.
- Skin
- Mm
- Hair
- N.S.P.

* Cut. manif.:

(a) Incid. : May occur in (25%) of cases of Sarcoidosis & the only affected by it in the 25%

(b) onset: →
- (in) 25% → Cut. manif appear before System.
- 25% → systemic manif before Cut.
- 5% → Simultaneous.

Cut. Sarcoidosis

Specific
(Shows Chic granuloma on Biopsy)

- Classical Presentation → (SKIN) "كفظ كويس جدا"
- Clinical Varities

Non Specific
(Reactive changes)

"مهم" ← EN (Most Common).
- EM
- Clubbing of finger
- Calcinosis Cutis
- Ichthyosis
- Pruritus
- Discoid Ecz.
- General Symptoms: fever, chills, wt loss, Fatigue.

Papular (miliary) Sarcoidosis (Common at Presentation):

Papules
- painless
- Sid: skin Colored, Red-brown or Violaceous, Hemispherical or lichenoid
- Surface: Variable scaling & umbilication
- Site: may be localized (or) Generalized
- Commonly: Bilat. & Symm.

(حفظ انكم كويس) لأنها مهمة → at
- Face
  - eyelids
  - alae nasi
  - Nasolabial
  - malar fold
  - Lips
- Neck
- upper Trunk & Extremities.

- on Diascopy test: "apple jelly" Color. [yellow-brown Spots]
- Fate
  - Coalescence → annular plaques
  - disappear → Pale, yellow or Telangiectasia, Scar

مهم · DD of Papular Sarcoidosis ??
- LMDF
- Granulomatous Rosacea.

Clinical Varieties = Great Imitator (Never vesicular / pustular)

- The lesion in Sarcoidosis instead of being papular It may be:

1. plaque (2nd Commonest type)
2. Annular. (Central Clearing & Peripheral ext. → Circ. Alop.)
3. S.C (Darier Roussy) Sarcoidosis: painless, Movable S.C Nodules + ± Systemic effect
4. Angiolupoid (± Marked Telangiectasia).
5. Morphea form (± Marked Fibrosis)
6. Scar Sarcoidosis: on top of Scar or old tatto → Infiltration → inflamm → Keloid like.
7. Lupus Pernio (Purpule Lupus).

   Insedious onset of: Indolent, Soft-doughy & Indurated, Purpule-dusky Violaceus Nodules & Plaques that effect areas Exposed to Cold

   - Nose
   - Ear → at the Rim → (Notching)
   - Cheeks
   - Scalp
   - Fingers

- Complication → Nose: Swelling, Ulceration, Crusting → dyspnea.
  → Fingers: Fusion, Swelling
  → Scalp: Scarring Alopecia.

8. Hypopigmented infil. Hypopigmental patches
   - a) ulcerative.
   - b) Erythrodermic & Ichthyosiform Psoriasiform

- What is the Significance?? "Spec"

Significant affection of:

- Lung: 75%
- URT: 50%
- Bone (Punched out granulom. atous lesions): 43%
- ocular: 37%. (chr. Uveitis)

- Mucosal Sarcoidosis.

Pinhead sized papules ± grouped → plaques.

- Sarcoidosis of Hair : → (Alopecia) ± d.d

  - Plaques that extend to scalp (annular)
  - Lupus pernio.
  - Macular lesions of scalp.

- Sarcoidosis of Nail. → Clubbing*
  → Subungual Hyper-Keratosis
  → onycholysis.

NB: childhood Sarcoidosis, usually presented ē

Arthritis

Cut. manif. — Uveitis

Less commonly Lung affect.

. less incid. of Lung.

| Non Specific Cut. manifs |

> So consider Sarcoidosis in any child complaining of Arthritis ē eye affect.

[illegible] → EN
- Commonest non specific cut. manif.
- similar to usuall EN.
- may be part of (Lofgren's Synd) [illegible]
  - Fever
  - Hilar L.N (BHL)
  - Arthritis (or Arthralgia)
  - Uveitis
  - EN

[illegible] أفضل نوع → (EN)
لل Sarcoid مع
EN لوحده

[illegible], its presence in cases of Sarcoidosis.
↓ ??
Good Prognosis (80% chance of resolution on 2 ys).

أسوأ نوعين
. SC
. Lupus pernio
أفضل نوع ؟؟

Systemic Sarcoidosis.

① **Lung** (90%) :
- Stage I : → Bilat. Hilar L.N (B.H.L)
- Stage II : → as I + Parenchymal affect^n
- Stage III : as II + Infec. / fibrosis / Pulm. insuff.

* Clinically : Cough, dyspnoea, Hoarseness,* Nasal obst & Sinusitis.

② **Liver** : Enlarged ē ↑ Enzs. (Severe affection is rare).

③ **Renal** : Hyper calciuria >> Hypercalcemia → Nocturia, polyuria, polydypsia, Nephrocalcinosis, RF

مهم d.t : ↑ Vit D Synth. by granulomatous Histiocytes. → "Renal stones."

④ **Musculo skeletal** (more ē Lupus pernio).

(i). Joints → Polyarthritis

(ii). ms → DM (Dermatomyositis) like

(iii). Bone → Bony Cysts of Hands & Feet.

** مش مهم

⑤ **Eye** :
1. Uveitis (commonest) (ē Heerfordt's synd, Lofgren's synd & Lupus pernio)
2. Conjunctivitis
3. Kerato conjunctivitis Sicca. (↓ Lacrimal sec. + Parotid enlargement). "KCS"
4. Eyelid oedema & Swelling : Lymphatic obst.
5. Dacroyostenosis
6. proptosis.

⑥ Parotid Enlargment: SS

[A] . Mikulicz Synd → Bilat. involvement < Parotid, Lacrimal, Submand., Sublingual
(KGs, SS) → Xerosis (Sicca Synd)

[B] . Heerfordt's Synd: (UVeoParotid fever)
. Fever
. Uveitis
. Parotitis
(Bell's palsy)

. Bell's palsy:
. HZ
. Leprosy
. Sarcoidosis
. Melckerson-Synd.

⑦ Heart: HB, arrythmia & death (Sarcoidosis of Heart is a leading Cause of death in Japanes).

Most Common is Cranial Neuropathy → ⑧ Nervous: Granuloma of < Facial N. / optic N. / Spinal Cord. → Palsy / Migrain.

. Cause of death: Renal, Cardiac & Pulm. affect. Incid (3%)

(art) Investigations of Sarcoidosis

كيفية التعامل مع أي حالة

Skin Invs

1. Biopsy.
2. Kveim Test.

Systemic Invs

1. CXR < Lung affection / L.N " / Cardiac " ± Feet & Hand XR
2. Pulmonary function tests.
3. LFTs & RFTs
4. CBC anemia d.t < BM affection / Chr. Course; leukopenia, Thrombocytopenia
5. Slit lamp Eye Exam.
6. Ca+ < Hypercalcemia. / Hypercalciuria.

Imp. → ⑦ Markers of dis. activity (ACE)

. ACE ↑ in: (DM, Alcohol, TB, leprosy, MAC)

⑧ Others: ↑ ESR, lymphopenia, ↑ Igs
↑ CD4/CD8 > 3.5 = Suggestive of Sarcoid.

⑨ ECG

Histopathology (Reticulin Stain)

مهم جدا تحفظ كويس

*upper & Lower dermal, **Non Caseating, **Naked ****Epitheloid Cell granuloma or Tubercle

*NB:
- L.V: upper dermal
- TT: lower dermal

**Not as TB (No central cheesy material)

هاما:

***Absent or Sparse Lymphoid Cell.
(by L/M this → Lymphoid but: by immunohistoch. → monocytes)

****: Cells:
- Epitheloid Cells.
- multinucleated Giant Cells: usually of Langhans Type ([illegible])

Epitheloid Cells may Show

Schaumann Bodies

(Basophilic Mulberry like).

- Rounded, Laminated, Basophilic inclusions (Mulberry like) توت.
- at first intra cellular then Extracellular.
- Represent: degenerating Lysosomes.

Asteroid Bodies

- Stellate, Eosinophilic inclusions
- Represent: Engulfed Collagen.

NB:
Both are non Specific for Sarcoidosis

NB

Chics of L V Pathology (ﻣﻬﻢ ﺟﺪﺍً ... L.V ...)

- upper dermal
- Scanty Caseation
- Absent bacilli
- Dense Mononuclear infil. (but Naked)
- Epid. Changes — Atrophy, ulceration, Acanthosis, Pseudo epitheliomatous Hyperplasia.

+ve — Kveim test, Tuberculin, Culture, Guinea pig inoculation.

(Stain) ZN

• DD: of Tuberculoid Granuloma

DD: Similar histopathologic features are present in: TB, Tub. leprosy, deep fungal infections, beryliosis, cut. leishmaniasis.

- LV: The infiltrate is located close to epidermis, marked inflammatory reaction around and between the granulomas, more central necrosis and epidermis shows either atrophy, ulceration, acanthosis or pseudo-carcinomatous hyperplasia. Also, Kveim test, tuberculin test, tissue culture and guinea pig inoculation may be helpful.
- Tuberculoid leprosy: The granulomas follow nerves and therefore appear elongated and more central necrosis.

LTS

	Lupus vulgaris	Tuberculoid leprosy	Sarcoidosis
Site	Upper dermis	Lower dermis	Upper & lower dermis
Shape	Rounded or oval	Elliptically elongated	Rounded
Adnexa	–	Involved	–
Caseation	±	–	–
Lymphocytes	+	+	–
Epidermis	Atrophy, Ulceration, Acanthosis, PEH	–	– / atrophy
Fibrosis	++	–	+
Special stain	ZN	Fite	Reticulin (Foot Stain)

"ﻣﻬﻢ" → Special stain

to Stain Reticular fibs around granuloma

- Foreign-body granuloma: polariscopic examination helps diagnosis.
- Acne rosacea resembles papular sarcoidosis but the infiltrate is perifollicular.

Gold
Sh
Shap.

Kveim test (Kveim-Siltzbach test):

تحقن وتأخذ عينة

- intra dermal injection of Heat Sterilized "Spleen of Infected Patient" → suspension of sarcoid tissue → 2-3 wks → Papule that Enlarge gradually then Reach maximum size → 4-6 wks (Highest activity of dis.)

- If No papule: The area is excised for Histological Exam.

- This test is +ve in: 80-80% of cases of Sarc.
  - -ve in: Patients going to remission
  - False +ve: = 2% (So it's Quite Specific)..

- NB: Not done Newders at risk of Inf. after Tissue inj.

- Markers of disease Activity:

  - ACE (↑ activity → ↑ level.. also may ↑ in: TB, leprosy, silicosis, MAC)
    - Secreted by granuloma
    - Correlate ē granuloma load
    - Specific & Sensitive (but)
    - No prognostic value
  - IL2R-1
  - beta → B2 microglobulins
  - Soluble IL2 Receptor & TNF II Receptors
  - Collagenase
  - Fibronectin
  - Neopterin

Prognosis of Sarcoidosis:

- In General → Resolve without Relapse
- 20-30% → Some permanent lung damage.
- 10-15% → Chr. Sarcoidosis that last for many yr.
- 5-10% → Fatal if affect vital organs.

"أي" → 60% of cases of cut. sarcoidosis resolve without treatment in 1-2 yrs especially those patients with EN or with Löfgren's syndrome.

Tt of Cut. Sarcoidosis

(depend on ① Symptoms
② Severity
③ Progression ④ disfigurement)

if

- **Asympt., mild, Non progressive, Non disfiguring**
  → Follow up for Spont. Resolution. (50% ē in 1-2 Ys) - Sp. GN

- **Sympt., Severe, Progressive, disfiguring dis.**
  → Corticosteroids (أم طب علاجي)

→ **Cut. Sarcoidosis**

localized

- Topical Cs
- intralesional Cs
- (intralesional Chloroquine)
- Topical Calcineurin inhibitors (Tacrolimus)
- Surgical
- Pulsed dye
- Co2 Laser

Generalized

1. Low dose prednisolone (EOD Regimen)
2. Other lines of Tt:
   - Antimalarial
   - minocycline
   - Allopurinol
   - Retinoids
   - MTX
   - Thalidomide
   - PUVA "new"
   - TNFα inhibitors (infliximab & adalimumab)
   - Cyclosporine.
   - Levamisole.
   - Colchicine.

MTX
3 — Antima.
Tetrac.
+
(PAT) — PUVA
Allopurinol
Thalidomide.

→ **Systemic Sarcoidosis**
→ **Systemic Cs**

1mg/Kg/d prednisolone for 4-6 Ws Taper over ms - Ys as dictated by "Systems affected"

NB . Cs dose : 40mg/d For several Ws → gradual ↓ to 15 mg EOD

. Lupus pernio : Cs + MTX or PDL . or Alefacept.

. Ocular SarCoid: لازم يتعالج هي لو مفيش اعراض لا → Blindness.

Palisading Granulomas

* Def. → subtypes of Necrotizing Granulomas ch By Central Zone of altered (degenerated) Collagen (Necrobiosis) surrounded by Histiocyte arranged in Palisading Pattern

- Palisading = spindle shapped Histiocytes (focally) Radiated (around) the *periphery (or) the long axis of the Spindle Shapped cells & their Spindle Nuclei are:
  - // to each other &
  - ⊥ to the Central Necrotic area.

- Palisading Granulomas are: (♀ > ♂)
  - Neoplastic →
    - G. A (Granuloma annulare).
    - A.G (Actinic Granuloma).
  - 2 Necrobiotic
    - NBLD (necrobiosis Lipodica diabeticorum)
    - NB. XG (Necrobiotic Xanthogranuloma).
  - Infectious
    - Gout
    - R.N. (Rheumatoid Nodules).
    - Cat scratch dis.
    - Wegners Granulomatosis
    - Papulonecrotic tuberculide.

- NB: Non Infectious Granulomas
  - Sarcoidosis
  - Palisading
  - LMDF
  - Granulomatous Rosacea.
  - FB Granuloma.

Granuloma Annulare
(Pseudorheumatoid Nodules)

Def: Chr. Idiopathic, Self limited, Necrobiotic granuloma ch by papules arranged in an annular or Arciform pattern.

- Epidemiology:
  - Age: usually (60%) < 30 yrs.
  - Sex: M : F = 1 : 2 (F > M)

Localized < 30 yrs
Generalized < Peak 10 yrs
Peak 30–60
d-c Nod → 2–10 yrs.

- AET: Unknown, but ± d.t delayed Hypersensitivity Reaction (a) Unknown Ag ∞ ± d.f
  - Insect bite
  - Virus.
  - PUVA.
  - Sun Exposure.
  - Tuberculin test.

- C/P of G.A [No mm affect]

Classical presentation (localized GA)

Lesion: multiple, flesh colored (Pink – Violaceous) papules arranged in an annular or arciform plaques (+++) (80%)

Site:
- dorsa of Hands & feet
- Elbows & Knees
- rare in other sites

Fate: (75%) usually Resolve in 2 yrs but Recurrence occur in 40% (usually NO Scarring)

Clinical Varities

1. Localized (1–10 lesions)
2. Generalized (> 10 lesions)
   - Subcut. nodular → Pseudo Rh Nodules
   - deep destructive.
   - Patch (Erythematous Type)
   - Perforating
   - HIV ass.
   - Neoplasm ass.
   - Granuloma multiforme* (GM)

(2nd)

[Variety كل من تحت هذه]

Clinical Varieties

- **Generalized**
  - Age Bimodal < 10 Ys / 30-60 Ys.
  - Poor prognosis
  - ↑ incid. of Lipid abnormalities (ass) & DM

- **Subcut. Nodular:** (Pseudo Rheumatoid Nodules)
  - usally in children
  - S.C Nodules at: Palm, Soles, Head, buttocks & Legs.
  - Looks like Rheumatoid Nodules

- **Deep destructive:** may destroy underlying structures.

- **patch (Erythematous):** Patch: Erythematous, Infiltrated, non annular. (MF like / Morphea like).

- **Perforating:** Papules show Central umbilicat. / plug. / Crusts. when squeezed → Little, Clear, Viscous Fluid —heal→ (Pigmented Scar.)
  - Represent: Transepidermal Elemination, Phenomenon.
  - ± ass. ē (HZ.) Scars (Wolf's isotopic phenom.)

- **HIV associated:** at any stage.

- **Neoplasm** ~ :
  - → ass ē Leukemia & Lymphoma.
  - → painful (!)
  - → unusuall location (Palms & Soles)

- **Granuloma multiform:** (Leiker) (Mkar dis.)
  - Limited to Central africa.
  - More in ♀ > 40 Ys.
  - Affect Exposed sites.
  - DD: TT / Syphilid.
  - Pathology as: G.A (but) Prominent Multinucleated Giant Cells.

• Conditions ass. ē G.A

- Nepl.
  - DM → Type I = Juvenile
  - Hyperlipidem.
  - HIV
  - Neoplasms
  - HZ (Scar)
  - Mauricas Synd. →
  - NBLD
  - Sarcoidosis

• Mauricas Synd:

- GA
- DM
- Hepatomegaly
- Dwarfism

• **DD** (A) of Annular lesions
(B) of Palisading Granulomas

interstitial
Necrobiotic granuloma
Tuberculoid granuloma
(DD + ve Mucin + Eos)
→ (3 pattern) —— **Pathology of G.A**

upper & mid dermal

Granuloma Interstatial Pattern (70%) (Commonest)
(infilerative granuloma)

- Seen in
  - Early lesions
  - Some fully developed lesion at edge of lesions.

↓

(i) Interstitial Histiocytes.
(ii) ↑ Mucin (Basophilic by Alcian Blue)
(iii) Intact. Collagen.

• Palisaded Granulomatous Pattern
(Less common)

Seen in fully developed Lesions.

• Center
1. Necrobiosis (altered Collagen or degenerating)
2. Mucin deposition:
3. Vascular Changes:
   - Fibrin
   - C3
   - IgM
   ] By Im. Flu.

• Periphery
Palisaded Histiocytes ē Few inflamm. Cells, Epithelioid Cells & Giant Cells

of G.A

① Reassurance (No ##): as Most Cases (75%) are self limiting ē in 2Ys.

② For disfiguring Cases:

- **Localized lesions:**
  - **## of Choice**
    - Topical or intra-lesional CS. (Superpotent)
  - **Other lines**
    - destruct By
      - Cryo
      - Laser
      - Radio
      - surgical
- **Generalized lesions:**
  - **## of Choice (Best)**
    - Isotretinoin
    - PUVA
    - Tetracyclines + Nicotinamide
  - **Other lines**
    - Dapsone
    - Antimalarial
    - Pentoxifylline
    - Thalidomide

Actinic Granuloma (AG)

(AEGCG = Annular Elastolytic Giant Cell Granuloma)

(Miescher's Granuloma of Face) (O'Brien's dis)

. usually Female > 40 ys.

. C/P: Annular Plaques:

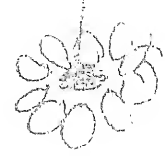
- Asymptomatic
- Border: Elevated & Erythematous
- Center: slightly atrophic & Hypopigmented
- Site: Sunexposed Sp. < Head / Neck

. Pathology: 2 Varities

- Interstitial Pattern (Common)
  ↓
  non palisaded (Interstitial) granulomas ē (FB) Giant Cells & Lymphocytes.

- Palisaded pattern (Rare)

(Central zone of Elastolysis)



*NB: differs from GA in:

1. more FB Giant cell.
2. No Central Necrobiosis (but Central Elastolysis). ← as GA [Show < Necrobiosis / Mucin]
3. No Mucin.
4. No lipid. ← as NBLD
5. Elastolysis (loss of elastic tissue in center of lesion)
6. Elastophagocytosis (elastic fibs seen inside Macrophages).

[illegible]

[illegible] :
* No < Necrobiosis / Mucin
* +ve < FB giant / Elastolysis / Elastophagocyt.

NB: Elastic fibs stain "Verhoff Van Giesson"

Treatment
↓
(i). Isotretinoin
(ii). Tetracyclines + Nicotinamide
(iii) PUVA.

Necrobiosis Lipoidica (NXBL)

• Def. Rare, Benign, necrobiotic disorder, affecting diabetics & prediabetics.

• Epidemiology:

. Age < non diabetic: 20-40 yrs. / diabetic: 50-60 yrs.

. Sex: M:F = 1:3 (F>M)

• Aetiology: unKnown, but ± [...]

① Related to diabetic microangiopathy

In one study → 171 patients of NXBL:

. 60% → diabetic (type I)

. 30% → prediabetic (High Risk ← abnl GTT / developed later)

. 10% → No Risk & No FH. (No FH)

Incid: it affect 0.3% of diabetics (3-7/100)

② Immune Complex (Vasculitis) suggested by IgM & C3 deposition in 50% of Cases.

• clp → Early lesions start as dull red asymptomatic papules & plaques → slowly Expand & may Coalesce → annular plaques.

. Center: yellow-brown, atrophic (+) Telangiectasia.

. Edge: Violaceous & may show HyperKeratotic Plugs (Represent Transepidermal Elimination phenomenon).

. Slowly progressive & Tend to heal ± Scar.

tibial) Commonest sites: Shin of Tibia but may also affect: ← thigh, Hand, Feet (as G.A) or scalp → atrophic patches

· Pathology: · affect all dermis & extend to S.C.T
Diffuse palisaded & interstitial Layered Tiers "granulomatous dermatitis" aligned // to skin surface. [palisading]
Lipid deposit.
[· +++ < Necrobiosis, Vascular changes; · No mucin]
· Superficial & deep perivascular, Lymphocytic infilt.
· Epid. → NL or atrophic.

Border

· depth →
· layered Ties //
· Necrob. ++
· Lipid.
· plasma Cells.

NB: this palisaded granuloma as G.A but differs in;

(1.) Granuloma is — Larger; more diffuse; more deep (deep dermis & S.C.T); Horizontal Tiers.
(2) More marked → Necrobiosis. → Vascular changes (C3 fibrin IgM) → plasma cells *
(3) Lipid deposition (Oil Red O stain & scarlet Red stain)
(4) No Mucin.

· +ve, lipid
· -ve: Mucin.

Treatment

(1.) Control D.M (usually no significant effect)
(2) Cs → Topical: for Early lesion. → ILs: for active border.
(3). Excision & grafting.
(4) Aspirin

• Necrobiotic Xantho-Granuloma (NB-XG)

(Class II Histiocytosis)

• Def → multi systemic dis. chronic:

• Cut. manifs:

① Periorbital: Xanthelasma like plaques & Nodules (orange (yellow))

but < deep Firm → may extend to the orbit → Eye < iritis, uveitis ✓ / Ectropium ✓ / Proptosis ✓
< indurated

② Trunk & proximal Extrem:

orange-red, plaques < active borders
atrophic center
± Telangiect.

That → may ulcerate.

③ ± Acral Nodules.

• Systemic manifs.

↓

- dysproteinemia (IgG monoclonal)
- dyslipidemia

- Leukemia
- Lymphoma
- LN
- HSM

• Histopathology: 1. Necrobiosis = Extensive
2. Palisading Granuloma ± foamy & Touton-Giant Cells. "ag"
3. Cholesterol clefts "ag"
4. Extracellular lipid deposits.

(tt) → Directed to Paraproteinemia:

- Cs ✓
- IFN α-2b (3-6 MU ✗ 3/w)
- Eye Radiation
- Nitrogen Mustard

Cat. Scratch dis

- Cat bite/Scratch $\xrightarrow{3-30d}$ Crusted papule or Nodule (ulcerat)
  $\xrightarrow{3-12\ w}$ Subacute Regional L.N (± suppurate) $\xrightarrow{2-6\ w}$ Resolut°

- Etiology: ± chlamydia

- Ttt: (1) Antibiotics → Not effective. (2) Cs: Contrary symptoms. & relief L.N

Gout

- disorder of Purine Metabolism ch by:

- ↑UA
  ↓
  ↑ deposit: (M) SKin, cartilage, tendon, joint.

- Hyperuricemia.
- Recurrent arthritis
- urate deposition in: Cartilage & skin (Tophi) → ag: Ear/Rim, DIP
- Renal dis.

Pathology

urate crystals surrounded by palisaded Histiocytes & mononuclear cells.

Wegner's Granulomatosis

(See Vasculitis)

- Granulomatous Respiratory Tract destruct.
  - focal or diffuse Glomerulitis
  - Necrotizing Vasculitis & Granulomas
    ↓
    usually → oral ulcerat ± Nodule

(Palisaded granuloma).

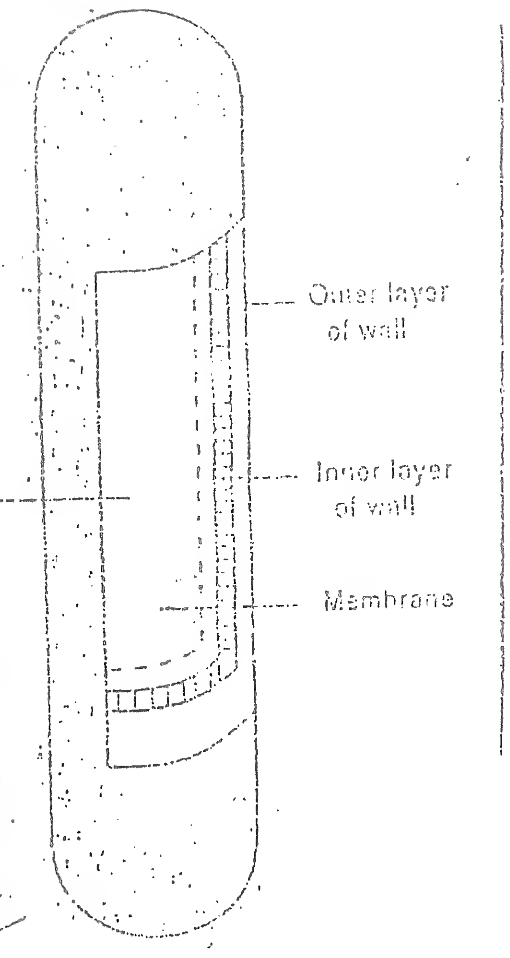
9/(2017) **Leprosy (Hansen's dis)** (١٨٧٣) ①

def. Chr. infectious, granulomatous dis. primarily affecting the peripheral Nerves (العرية سرغر) & (Secondarily) involving The skin & mm (of URT) & Certain Other tissues specially:
- Eyes;
- Testes.
- Bones
- Liver.

Cold Areas (35°C)
- Nose
- Testes
- Ear lobes
- sup. NS

AEt: Mycobacterium Leprae;
- obligate intracellular parasite of Macrophages & Schwann cells → طفيلي داخلي → Inoculate / Stain / Culture
- Acid fast & Alcohol fast but < MyCob. TB (Gram +ve)
- Non culturable but can be inoculated in
  - Mice foot pads &
  - Nine banded Armadillo.
- Stain: by Modified Ziehl-Neelsen (ZN)

1.8 μ x 0.3 μ



Schematic structure of Mycobacterium leprae

Susceptible individ + Open case of Lep.

Structure
↓
has Capsule that is formed of 2 lipid layers

① phthiocerol dimycocerosate:
Non specific & Shared by other organism.

② PGL: phenolic Glycolipid Coat:
- Specific for M. Leprae
- responsible for:
  - Binding to G-domain of α chain of laminin 2 of basal lamina of Schwann cells
  - difficult Staining ↰ d.t. "Waxy Coat"
  - Foamy Macrophages ↲
  - ++ TLR₁ & TLR₂ (on surface of Schwann).

* **Epidemiology: (2011)**

- **Age**: Bimodal
  - Peak: 10 – 15 ys. (children are at greater risk)
  - also ": 35 – 45 ys
- **Sex**
  - Adults: LL > TL & M > F (2:1)
  - Children: TL > L.L & M = F
- **mcid**: Tropical & sub tropical areas.

M=F

Mode of infect^n

* Requirments or Transmission:

[1] Contagious Patient (open case ē multibacillary)

[2] Close or Intimate Contact

[3] Suceptable person [predisposing factors]

* Mode of Transmission:

Main mode: (droplets)

- **Exit** < Nasal / oral droplets (May remain viable on dried sec. for 1–7 ds)
- **Entry** <
  - usually: Nasal mucosa or oral mucosa
  - less common: breaked (Abraded) skin

Less Common Modes:

- Eroded skin
- Blood
- Faecoral
- Transplacental
- Breast feeding

IP: 3 – 5 ys (may ± short 1.5 y or longer 15 ys) (TL ≃ 4 ys, L.L ≃ 10 ys)

Predisposing factors for development of inf.

1. Genetic <
   - HLA DR2 & 3 → TL
   - HLA DQ1 → L.L
2. Endemicity → مصر كانت موجودة
   الهند - البرازيل - بنجلاديش
   نيجيريا - اثيوبيا
3. +ve FH
4. Overcrowding
5. Poor sanitation

Absence of these factors → usually NO dis.

Pathogenesis of Leprosy.

(Most) people Infected ē M. Leprae develops a "Subclinical" infection >> & recover. Naturally (A) few people "who are" susceptable >> → develop the dis.

- Genetic
- Endemic
- FH
- Poor sanit- & Crowding

M. leprae has predilection for "neural tissue" (Neurotropism)

↳ reaches the "peripheral" nerves via: Endo & perineural BVs:

↓

Schwann cells (Target Organ)

- In patients ē High Immunity (as proved by lepromin test) (TH1)

↓

++ Th1 (predominates)

↓

IL2, IFN-γ, TNF-β

↓

++ Macrophages (IL-12, TNFα)

↓

Efficient digestion & destruction of the bacilli

↓

- The reaction remains localized to the nerve (out spread to skin) = pure Neural leprosy.

or

- The reaction spreads to the skin "only" [peri-neural]

↓

Epethiloid granuloma

↓

Tuberculoid Leprosy (TT)

- In patients with Low Immunity (as proved by -ve test)

↓

-- Th1 (by the cytokine coat)

↓

Th2 predominates

↓

IL 4, 5, 10, 13

↓

-- Macrophage

↓

① Little Lymphocytic infiltration

② No Localization of inf. → Spread to skin & other organs (diffuse infil.)

③ Bacilli Invade & Accumulate inside & outside the Macrophages

↓

Foam cells or Lepra cells

↓

(Multibacillary)

- In Both types No bacilli are detected (Paucibacillary leprosy).

• Classificat° of Leprosy

I. Ridely & Jopling: clinical classificat° (spectrum)
II. WHO Classificat°: Therapeutic " (Pauci & Multi).

Ridely & Jopling classificat° (Spectrum of leprosy)

CMI → ↓↓ Toward L.L
Humoral → ↑↑ " " "

IL (indeterminate leprosy) — TT (Tuberculoid Leprosy) — BT (Borderline Tuberculoid) — BB (Border line Border line) — B.L Borderline lepromatous — L.L Lepromatous leprosy →

IL: early ↓

- Transitory stage in those ē undetermined Immunity.
- May remains for (ms - ys) then either
  - Resolve spont. (75%)
  - Progress To any Type (weak Immunity).
    - if ↑↑ Lymphocyte → TT
    - if ↓ T cells & ↑ Bacilli → L.L.

. We have 2 Polar Forms (stable) [TT, L.L] (نفيش فرق مرم بيكل للتاني)

. the Other Forms < BT, BB, BL unstable Types

May ē < good IH → go Towards TT; Bad IH → go " L.L

. Indeterminate leprosy

- Early (initial), Transitory manif. of leprosy that occurs in patient ē undetermined Immunity
- usually affects children.
- C/P. single or few Hypochromic or Erythematous Macules usually ē NL Sensat°.
- HP: Non specific Inflamm. Infilt.
- Bacteriology: Few or No - Bacilli
- Immunology: variable Results of Lepromine test.
- Fate: see Above.
- TTT: According to its progression.

	Tuberculoid Leprosy	Lepromatous leprosy.
CMI	• occurs in patient ē Very high Immunity	• occurs in patients ♂ Very low Immunity (No Resistance).
Organs	• affect only Nerves & Skin.	• Can affect: Nerves, Skin, ex: mm, RES, Testes, Eye.
Infectivity	☺ Non infectious (±)	☹ infectious.
IP	• mean: 4 Ys.	• mean: 10 Ys.
Skin lesions	• Usually: Single or few (<5) & Asymmetrical. • usually: plaque or patch But may be macular - single or few, Asym., erythematous or hypopigmented with well defined Elevated borders ē tendency to central clearing (Saucer right side up). ☹ There are loss of: • Hair → dry, hairless • Sensation → Anaesth. • Sweat → Anaesth. → Usually affect: Face, limbs, Trunk, buttock • The Superficial nerve in the Vicinity of lesion ± palpable. (5) Ear lobes infil. (Elongated soft)	• Multiple, Bilat. Symmetrical without: loss of hair, " of Sweat, " " Sensation • There are 3 types: (a) Macular: Multiple, Erythe. or Hypopigm., ill defined (b) Nodular: Skin colored, Pink to Coppery Papules ē smooth & shiny overlying skin. (c) Lucio type (diffuse) (d) Histoid Type: NB L.L may → (1) Leonine Face (2) Madarosis: loss of outer 1/3 of Eyebrow (3) Ichthyosis of L.L (4) Saddle Nose. any area can be affected Except Warm areas. (Folds, scalp)

(N.B.) Earliest Manifs of L.L:
Is Skin & Nasal (stuffness, discharge & epistaxis)
Epistaxis ... أول أعراض

	TT	LL
Nerve affect	- Nerve affection is: Early, Single - Confined to skin lesion or Peripheral NS	N. affection is: Late (3-4 s), multiple, Bilat. & Symm. • Not ass. c skin lesion

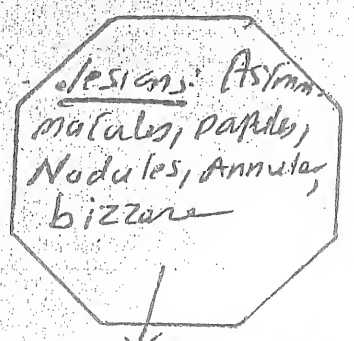
(i) Sensor
(ii) Motor
(iii) Autonomic → lost ← Hair, Sweat, Sebi.

• Manifs. of Nerve affect:
⇒ Sensory N. → dysthesia, paresthesia & hypoesthesia (stock & glove) Neuropathic ulcers
⇒ Motor N. → ms weakness (Foot drop & Claw hands), wasting & Trophic changes → osteoporosis & Bone Resorption
• Exam: thickened, Nodular & Tender.

Other organ affect	• No affection to other organs.	• Affect other organ: - liver, spleen: Low - Kidney - Testes → Orchitis → Gynecomastia, sterility - Eye → Lagophthalmos (4th), Corneal & Conj. anesth. (5th) also: Uveitis, Iridocyclitis, Glaucoma • MM: Nasal U/Crust, Epistaxis, Saddle Nose & Hoarseness. • Oral: Papules, Nodules at palate, Gum, Lips (Palate perforat), Teeth falling
Histopathology	(Epithelioid Cell granuloma)	(Virchowcytic Granuloma)
Bacteriology (Skin smear)	-Ve (No Bacilli)	+Ve (Large No of bacilli)
Lepromine test	Strong +Ve.	-Ve
Immunology	• ✓ Good CMI. • Low HI (Low Antibody titer than LL)	• ↓↓ CMI • High HI (Antibodies detected in high titer but of no role cuz they can't attack Intracellular organism) + but H.I: play role in Type II react.
Reaction	• Usually No	• Usually Occur.
Prognosis	Good / Stable Course.	Poor / liable to Reaction

Border line leprosy

- Immunologically unstable (either regress to TT or progress to L.L).
- No Systemic effects
- Clp, Bacteriology, HP, Lepromine test ~ TT & L.L بين



Punched out or Swiss cheese plaques (Chic of BB).

	High Resistance	Unstable resistance (Dimorphic)			No Resistance
	TT	BT	BB	BL	LL
Lesions	1-3 (<5)	Few	Few or many Asymm.	Many + Symm > Asymm	Numerous & Symm.
Bacilli smear	–	1+	2+	3+	4+
Lepromine test	3+	2+	+	+	–Ve
Histopath.	• Epithelioid cells decreasing → • Nerve destruction (Sarcoid like granuloma)			• Histiocytes, foam cells, granuloma (Xanthoma like)	

• Nerve effects in leprosy:

(i) Sensory Nerves: Most Commonly effected are UMRGsp (Ulnar, Median, Radial, Greater auricular, Superficial Peroneal, Lat. popliteal & Post. tibial).

ولد. Why Ulner N. is the most Common

Sensation loss:
- Temp
- Light T.
- Pain
- Deep T.
- Pressure.

(i) prominent Schwann (35°C)
(ii) superficial → Cool → Suitable for M. Leprae.
(iii) over bony prominence → liable to trauma → devitalization of N. Tissue.

(j) Motor Ns: rarely affected (deep → High temp).

(jj) Cranial Ns: 7 out of 12 Intra Cranial Course → High temp. 2, 5, 7 except olfactory (2). Trigeminal & facial.

• Special Types of Leprosy

(1) LuCio Leprosy
(2) Histoid Leprosy

• LuCio Leprosy (Pretty Leprosy = diffuse Lipromatosis)

• Type of L.L Thats Common in MexiCo Caused By M. Lepromatosis due to Total lack of Host Resistance.

• Cli BY: (1) Skin: diffuse dermal infiltration; so in old persons ē wrinkles on face → (smoothout) the wrinkles → youthful appearance. (So Called Lepra komita = pretty L.) (Scleroderma like)

(2) Hair: loss of < Body. eyelash. Brow.

(3) Sensat.: wide spread loss.

(4) Nasal, Laryngeal affect & wide spread Telangiect.

• Has Unique Reaction: (LuCio phenomenon)

• Histoid Leprosy..

• special Type of L-L. ± occur < de novo. or Relapse of L.L d/t discont. Tt or resistance

• d.t < Discontinuation of Tt (or) Drug Resistance (or) after Chemo Therapy.

Lysis 2D

• Clp
- Skin: DF like Copper or yellow-Red dermal & S.C Nodules ē (NL) Skin over it. Common at — Face, lower back, Buttock.
- Nerve → Abscess like Swellings. (Neural Histoid).

• Path: see before.

(تحويل) # Pathology of Leprosy (بولوتيا)

3 Basic Histological patterns are seen

- **Tuberculoid Pattern** (TT) → dermal granuloma (Tuberculoid ") or Epithelioid
- **Lepromatous pattern** (L.L) → diffuse infilt. of skin & other organs. (تخلل)
- **Borderline Pattern** (BT, BB, BL) → Patterns bet 1st & 2nd types

TT Pathology

↓

Dermal granuloma

- شكله → Elongated or linear. (Nerve ماشية جنب ال)
- مكانه → dermal along the course of the nerve. (Perineural) (حوالين)
- مكونات 1. Epithelioid Cells.
  2. Langhan's Giant "
  3. Lymphocytes (at periphery < Large No / T4 > T8)
  4. Bacilli: Absent.
- Nerve → destruction

مهم | D.D from other Tuberculoid Granulomas as Sarcoidosis By « Nerve inflamm. & Fragmentation »

ملخص علمي | Linear (Elongated), Perineural (dermal) granuloma Composed of ← (without) bacilli ass. ē Nerve destruction

(تذكيرها جلده) ⑩

L.L Pathology

- شكلها → diffuse infiltration.
- مكانها → deep skin & other organs e.g. Bone, Testes.
  - dermis
  - S.C.T

  Separating from the overlying epid. by well defined Grenz or Unna Zone (Zone of NL compressed Collagen).

- مكوناتها ① Virchow Cells (Lepra Cells or Foam Cells)
  Macrophage laden bacilli & Lipid droplets
  stain:
  - H & E: → Foamy.
  - Sudan IV → lipid appear orange

  ② Plasma Cells.

  ③ Lymphocytes:
  - Scanty
  - of T suppressor type (T8)

  ④ Bacilli: Numerous in dermis & have shape of:
  - Isolated,
  - globi, &
  - granular or fragment (under H) (Methenamine Silver)

- Nerve → Perineural concentric fibrosis (onion skin appearance).

Border line Path
Mixed virchow (LL) Tuberculoid (TL):
٣ أشكال

1) Some lesions show Virchow & others show Tuberculoid.
2) in same lesion
L.L pattern + T.L pattern
3) All lesions are mix of foam Cells & Epith. Cells.

NB: in Histoid Variant Well circumscribed Prolif. of Spindle Cells Containing bacilli that typically lie up along the Long axis of Cell. (whorled arrangement).

Pathology

• Stain For 3
1. Bacilli
2. Nerve
3. Lipid (Foamy cells)

• NB on the

the most diagnostic features are:

① Presence of bacilli (مهم)

Leprosy → ② Selective nerve destruction (by S-100 stain).

③ Perineural concentric fibrosis.

Bacilli

• Fruit Bud sites (أكثر أماكن تجمعها)

- Nerves
- Subepid. Zone
- Arrector pili ms.

• Stain:

Fite
- H & E
- Ziehl-Neelsen (أسفوي)
- Fite (أسهل وأجود تلوين)
- Wade

→ Bright Red

Scarlet red
- Sudan III → B-Pack
- Sudan IV → Red
- Methenamine Silver → "detect fragmented bacilli"

• if Scanty bacilli: before saying it's -ve
Take at least (6) sections.

+ Also Can be seen by PCR.

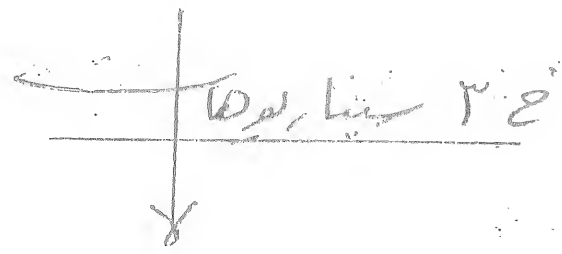
(VB)

• Pathology of Border line Patterns. (BT → BB → BL)

• Mix of both L-L (virchow cells) + Tuberculoid form (granulomas) ... the predominance of the Former versus the Latter is dependent upon whether patient has BL, BB or BT

BT ⟶ BB ⟶ BL

* Virchow cells → تنزيح هذا الاتجاه
* Granulomas → تنقل نحو هذا الاتجاه (Epithelioid)



(1) Some lesions are < as L-L & as TT

(2) Epithelioid & Virchow cells seen in same lesion

• Indeterminate Leprosy: difficult to be diagnosed. Histologically only some lymphocytic infiltrate present (No < Foam cells granuloma).

10

Reactions in Leprosy

(سؤال إمتحان) < شفهي / تحريري

(13)

Def. Acute Episodes (Reactions) that may occur during the chronic course of Leprosy

- They may occur Either
  - Spontaneous or
  - ppt BY:
    - ttt (after 4-6ms) ← Initiat
    - stress
    - Inf.
    - vaccinat
    - operation
    - pregnancy
    - parturition.

- there are 3 types of Reactions
  1. Type I :→ lepra reaction (Reversal or downgrading reactions.)
  2. Type II :→ ENL
  3. Type III : Lucio Phenomenon.

	Type I Reaction	Type II Reaction.
Type of Leprosy	. Mostly Border line Leprosy (BT, BB & BL) . Occasionally: TT. (rare)	. Mostly: LL (in 50% of cases) occasionally: BL (L.L & BL)
Pathogenesis	. Type IV Hypersensitivity React (change in CMI). . due to: (1) Initiat of ttt (after 6ms) → up-grading (reverse) (2) untreated Patient (downgrading) ~~(3) Spont, Purperium~~	. Type III Hyper Sensitivity (Ag + Ig + C → deposit in Tissue, BVs & Lymphatics) . due to: (1). Initiat of ttt (1Y) (2). Untreated Patient ~~(3) during ttt~~.
C/P	Triad 1. Acute Neuritis 2. Acute Dermatitis. 3. Acral Edema	Triad 1. ENL 2. Systemic Manifs. 3. Constitutional M.

ttt < Initiat / No ttt] I & II React.
discontinued → Lucio.

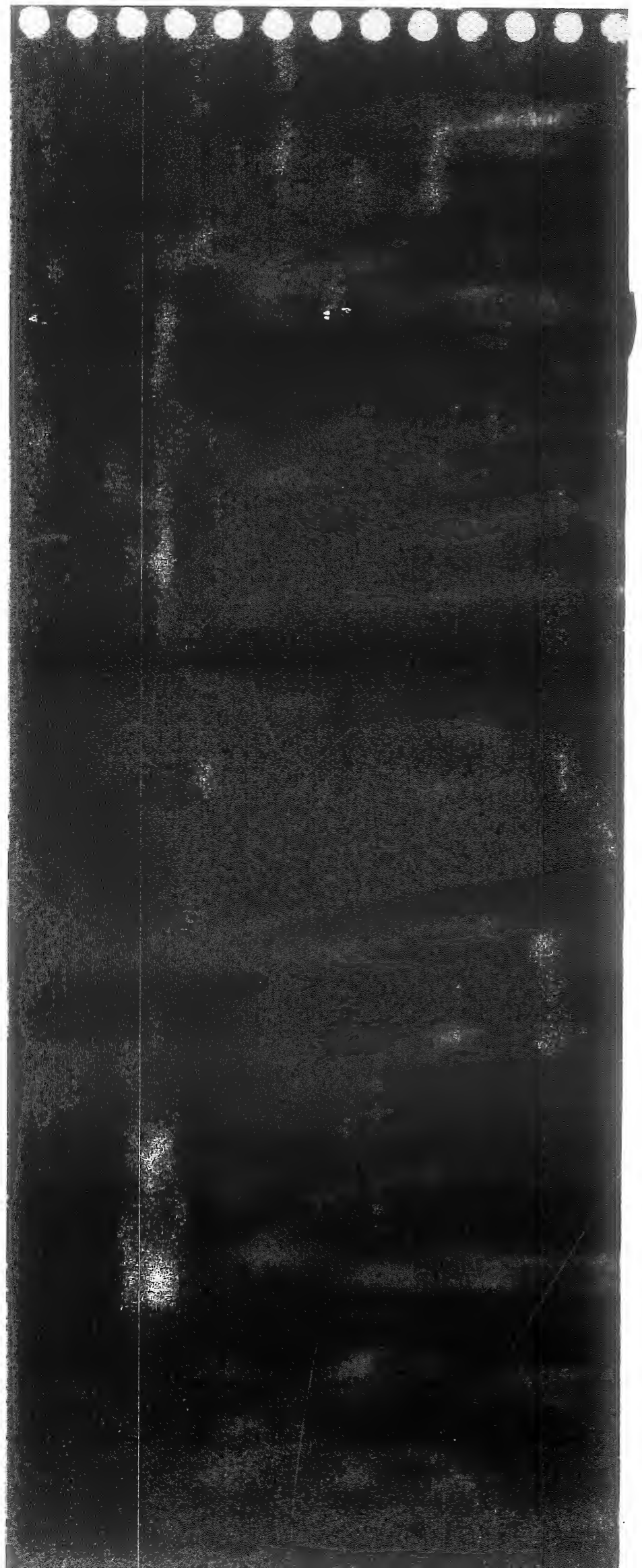
	Type I	Type II. "only"
Skin manif. (Acute - Neuritis & dermatitis)	• ē upgrading: lesion ↑ inflammat= & ulcerat= • ē downgrading: progression of lesion Towards L-L (the NL skin remains Intact)	• Affect° of NL SKIN (Existing lesions don't show clinical aggravat°). • There are: sudden onset & erupt° of Evanescent (lasting for days) Erythematous, Dermal-& S.C.T., Nodules ⓔ Generalized dist→ ulcera • ENL: may be → Vesicular, Bullus, Pustular (EN Necroticans), ulcerative: (1st manif. ⓒ lepr=sy
Nerve	Rapid Nerve Inflamm. (Acute Neuritis)	• Slow Nerve Inflamm.
Associations	• Oedema (ACral) of { Hands, Feet, Face } [± presenting SES.] • Neuritis & paralysis { Hands, Feet, face (7th N.) } → (Facial palsy) (ACral Edema ⓐ Paralysis)	• Iritis, Iridocyclitis, Glaucoma, Arthritis, MYOSitis, Bone Pain, Stridor, Glomerulonephritis. • ↑ESR, Leuco-cytosis, ↑IgG, C2, C3, Neutrophilia
Lepromin test	• +Ve in: upgrading reactions. • -Ve in: downgrading "	NO Effect
Histopath.	• in upgrading → (shift to) tuberculoid Pole • in downgrading → " → Lepromatous Pole	• LCV (Neutrophilic Leucocytoclastic Vasculitis ⊕ Scanty fragmented bacilli).
Treatment	Prednisone 20-60 mg ld (tapered by 5mg/24hrs For 24ms BT & 6ms BL) other lines: • Cyclosporine • Clofazimine (300 mg ld) 30	• Thalidomide (100-200 mg ld at night) other lines: • Cs (80 mg → rapid tapering) • Clofazimine (upto 300) • Pentoxifylline ± Clofazimine.

- Avoid pot. factors
- (2) continue tt of Leprosy as usual.
- (3) Prophylactic 300mg prednisone during 1st 3ms of tt.

NB

① . Type I reaction: Cs ③. Lucio → Cs

② . Type II : thalidomide



Lucio's phenomenon or Reaction

(اصطلاح) (5)

. Type of Reaction that may occur in diffuse L.L (Lucio Leprosy) So, Some Consider it as a type of ENL.

. differs from ENL in: (5)

"discontinuous Not initial"

1. initiated ē stop of ## (Not ē start)
2. No systemic manifs.
3. No Neutrophilia, or leukocytosis
4. ## → Cs
5. HP: LCV + dense Bacilli

. Clinically: ← Vasculitis (word)

. Thrombosis & Necrotizing Vasculitis of Small Vs → Purpura, Hge, bullae → Painful Erosion → Scar.

. usually: below Knee, buttocks, forearms.

. pathology → bacilli in skin & Necrotizing LCV

(##) → Cs

16

B Bacteriological Exam.

• Skin Smear

(Slit Smear = Bacilloscopy)

1. Routine in any suspected Case
2. Highly specific but Not sensitive. (30%) → Can't detect Conc. < 10^4/g Tissue)
3. Value
   - diagnosis.
   - Asses the Results
   - detect the most infectious pt

Technique (929) مطلوب

. Sites = Common sites of L.L

. 6 Routine sites ± others

- 2 Earlobes
- 2 Elbows
- 2 Knees

Others:
- Forehead
- Chin
- Trunk
- Buttocks
- Extensor Forearm ..

* لازم نحفظ الأماكن اللي أخدنا منها العينات علشان ناخد منها تاني بعد العلاج.

* في L.L ، عينة من كل الـ 6 مواضع

• Nasal Smear

(Not Routine)

Either By

- Nose Blow Smears — بيطلع الصبح بدري بينفخ في كيس بلاستيك وكده.
- Nasal Scrappings → . Not Used ??

(Slit smear) طريقة عمل

- lesion Cleaned ē Alcohol
- Fold is Picked up bet. thumb & forefinger → squeezed tightly To render it free of blood.
- Small incision is made in dermis (L: 6 mm / depth: 3 mm) → Turn the blade at right angle
- Fluid (Serum) collected at the angle (Not blood) → Fixed (air dried Not flam.) & stained ē Z.N

[bacilli appears red rods over Blue back ground]

- Bacterial Index (BI): density of bacilli in Smear.
- Morphological index: % of "Persumable" living bacilli in relation to total No of bacilli in Smear.

Grading of BI (أكيد)

Diagnostic clinical & Bact. Criteria

(Classification of Leprosy)

Bacilloscopy available (Slit smear)

- No bacilli → Paucibacillary L.
- +ve bacilli (even 1 bacillus) → multibacillary L.

Acc. To An Ethiopian Study

- If ≥ 1 of the following → Diagnosis of Leprosy:
  1. Hypopigmented or Reddish (Anaesthetic) Patches
  2. Thickened Peripheral Nerves
  3. +ve Bacilli

So Paucibacillary: is leprosy with ≤ 5 lesions & no bacilli in smears & include TT, BT

- Multibacillary → ≥ 5 lesions with or without

Bacilloscopy NOT Available

(Diagnosis in endemic areas)

WHO (1997)

[لو مفيش حالة .L وحبيت تشخص بسرعة ← عدّ الـ Lesions]

- ≤ 5 Lesions → (PB) Paucibacillary
  - (SLPB) Single lesion → ROM therapy
  - 2-5 lesions → MDT for 6ms
- > 5 lesions → Multibacillary (MB) → MDT for 2 ys

[يعني انت شخصت الحالة وعالجتها في وقايم معدودة]

كيفية قراءة ال
(Slit Smear)
C using 100 OIF)

(A) B.I = Bacteriological index "N"

عدد البكتريا الكلى فى كل عينة فحص (OIF)

(B) M.I = Morphological Index

نسبة البكتريا الحية الى العدد الكلى للبكتريا

1. Living = Solid
2. Granular & Fragmented = dead.

* With Tt : Bacilli disappear:

- BB : ein few min.
- BL : 1-2 hr.
- L.L : 5-10 hr.

Grading of BI		
6+	=	>1000 bacilli per OIF
5+	=	100-1000 bacilli per OIF
4+	=	10-100 bacilli per OIF
3+	=	1-10 bacilli per OIF in each OIF
2+	=	1-10 bacilli per $\frac{1}{10}$ OIF (10 Fields)
1+	=	1-10 bacilli per $\frac{1}{100}$ OIF (in 100 OIF)
0	=	No bacilli in 100 OIF

آخر مكان تفحص Bacilli منه ↓ dorsum of Hand.

NB

Bacilli present in

- 100% L.L
- 75% BB
- 5% BTF
- 0% TT

C Histological Exam.: (Biopsy)

Skin Biopsy

شرطين

- deep (to SCT)
- From: active Edge.

↓

"Fite-stain"

Nerve Biopsy

↓

done if there is No cut. lesions (pure Neural leprosy)

taken from Sensory N. (No risk of motor damage)

e.g superficial peroneal at dorsum foot.

D Clinical tests: (May aid in Ø; less frequently used Nowadays)

1. Lepromine test
2. Histamine test
3. Pilocarpine test

Lepromine test:

- Lepromine: is a crude "Semi-Standardized preparation" of bacilli derived from a Lepromatous Nodule ⊕ from Infected armadillo liver. (Heat Killed M. leprae)
- 0.1 ml Lepromine Intradermal injection & Examination is either done after
  - 48 hrs: → Fernandez reaction.
  - 3–4 ws: → Mitsuda reaction.
- if Nodule at site of inj. → +ve test.

- **+Ve lepromin test**

- **+Ve Fernandez reaction (Diagnostic)**

  ↓

  Indicate: delayed hypersensitivity reaction to: *M. Leprae* antigens or across reacting Mycobacteria.

  NB:

  - This test doesn't indicate Past or present Leprosy Inf.

  The test is:

  (i). Strong Positive → in TT

  (ii). Weak +Ve → BT

  (iii). -Ve → BB, BL & LL.

- **+Ve Mitsuda reaction.**

  (prognostic)

  - **+ve**

    means that the patient can have good CMI to Resist the inf. (TT & BT)

  - **-ve**

    Patient or Populations at Risk of Leprosy. (L-LepL)

NB « Patients ε LL Never Become Lepromine +Ve Even when Healed »

Interpretation of Mitsuda reaction

- Nothing: -ve.
- ≤ 3 mm papule: ± (doubtful).
- 4-6 mm papule: +
- 7-10 mm papule; ++
- ≥ 10 mm nodule or ulceration irrespective of size: +++

— 1 2 3 4

4+ 3 2 1 - no

Histamine test (to defect Nerve damage)

(Sympathetic Assessment)

- NLLY: Histamine ID inject → ++ Nerve
  → Flare (local axon reflex).

- Result ← NL Response: L.L (late Nerve affect)
  Absent ": TT (SW) (early)
  Weak or delayed: B B or Indeterminat Leprosy.

Sweat Function Test (pilocarpine test):

- Methacholine Test
- Apply Tr. Iodine to NL skin (control) & suspected lesion → then inject pilocarpine → then apply starch to these areas (will turn blue if +ve sweating).

(Para Sympathomimetic)

- Significance (only in non L.L) Why ??
  1. used in children in whom sensation can't be determined certainly
  2. Loss of sweating may precede Anaesthesia
  3. BlackS (Flare not seen by Histamine test)

Serodiagnosis:

(1). Antibodies to M. lepra Ags: highest in LL & lowest in TT (عنوان تقل)

(2). ELIZA: For detection of Antibodies against the phenolic dixolipid coat (PGL)
- useful screening.
- highest in LL & BL
- Low in TT
- ↓ during chemotherapy.
- ⊙ useful screening test.

(3). FLA-Abs: Fluroscent leprosy antibody Absorpt° test for detection of M. Leprae specific Abs.

(4). RIA: for Antibodies to Cell wall Ag of M. lepra.

(5). PCR: for detection of M. lepra DNA but (not) helpful to detect mild & early inf.

(MIB & early)

(حرابه) **Leprosy in 3 situations**

- children
- pregnancy
- HIV patients.

مهم **Leprosy in children ch' BY:**

(i) Children are at higher risk to develop inf from the family Infected ē Leprosy.

(ii) usually Paucibacillary ē single lesion localized To Face or buttock

(iii) Good prognosis ē ≥ 75% Spont. Resolut=

(iv) React= is uncommon.

(v) Dapsone: 1-2 mg/kg/d

Rifampicin: 10-20 mg/kg/d

Clofazimine: 1 mg/kg/d.

(vi) Short IP

مهم • **Leprosy & pregnancy**

• Effect of pregnancy on leprosy

1. Exacerbat=
2. Reactivat=
3. Reaction.

• Drug: 1. MDT: all (3) are Category (C)

2. MinoCycline (D)
3. Thalidomide (X)
4. ofloxacin (C)

Diagnosis of Leprosy.

(1) Clinical Examinat~ (Skin, Nerve, Diagnostic Criteria)

(2) Bacteriological Exam. (Slit & Nasal Smear)

(3) Histopathological N (Skin & Nerve Biopsy)

(4) Clinical Tests (Lepromine, Histamine & Sweat Function Test).

(5) Serological Tests (ELISA for detect~ of PGL abs & PCR).

أهم ٣ :
- SSS
- Biopsy
- PCR

A: Clinical Examinat:

• Skin Exam. (lesion / Hair / Sensat~)

lesion → Viewed (in good light / Directly & obliquely)

For Hair →

For Sweating →

Sensat~ → (تحسس كل واحد لوحده)

• Note TLPD (Temp – Light Touch → Pain → deep Touch)

at lesions / Distal Extremities

باستخدام: قطن أو دبوس وحاجة ساخنة أو باردة

• بشرح إختبار للمريض ونذوقه على عينه أولاً لما يبقى عينه مفتوحة ولما يتقفل بنعلم وهو مغمض عينه ونقارن بين الـ NL Skin & lesion وبين جانبي الجسم.

• Nerve Exam.

• Examine the nerve for:

1. Tenderness
2. Consistency
3. Size
4. Symmetry

• Affected Ns may be:

- Cord like (Thickened)
- beaded
- Abscessed.

(i). Ulnar N: → Palpate at inner side of Elbow (when Elbow semiflexed) Tender

(ii) Median → at "wrist when semiflexed.

(iii) Greater auricular: → head turned to opposite side.

(iv) Lat. popliteal: behind neck of fibula (e) Knee semiflexed.

* Most healthy show palpable Ns; so examine (for) Both sides & for tenderness.

• Treatment of Leprosy

- Tt of the dis.
- Tt of Reaction (سبعة)
- Others

- Chemotherapy (اهم واحد)
  - (i) MDT
  - (ii) USA DT
  - (iii) NDT
- 2. Immuno-therapy → "Vaccine"
- 3. Chemo-Immunoth.

• Chemotherapy

"اهم حاجة نتكلم عنها"

"Multiple" or Multi- → MDT

① • WHO "PT"

② USA "للبحوث فقط"

New Drug therapy
- Isoprodian
- Minocycline
- Fluoroquinolones
- Clarithromycin
- ROM

✓ ✱ Chemotherapy: Aim:
1. Stop infect
2. ↓ Morbidity
3. Prevent Complications
4. Eradicate the dis.

- Stopping & eradicate
- Prevent Complic & ↓ Morb.

• MDT regimen is designed to avoid bacterial resistance.

"PT" • Dapsone:
- Most important drug.
- Cheapest
- Bacteriostatic.
- adult drug dose 100 mg/d (1-2 mg/Kg).

"RIF" • Rifampacin.
- The most potent drug.
- Bactericidal
- dose: 10-20 mg/Kg/d (600 mg on Empty stomach 1/day).

(Render the pt ... rapidly).

• Clofazimine
- Slowly bactericidal. anti-inflammatory
- Effective as Dapsone.
- 50 mg/d/e Meals @ a glass of milk.

Rif. is Rapid bactericidal while Dapsone ...

B

(13)

MDT by WHO (Adults)

1. Paucibacillary (SLPB) (Single lesion) → ROM therapy (Single dose)
   - Rifampicine (600 mg)
   - oFloxacin (400 mg)
   - Minocycline (100 mg)

2. Paucibacillary (2-5 lesions): 2 drugs
   - daily Dapsone (100 mg at Home)
   - Monthly Rifamp. (600 mg under-Supervision).

3. Multibacillary (>5 lesions): 3 drugs
   - Daily (at home)
     - Dapsone
     - Lamprene (50 mg)
   - Monthly (supervised)
     - Rifamp. (600)
     - Lamprene (300)

Duration of Tt

- Paucibacillary (2-5 lesions): For 6 ms & Follow For 2 Ys (Relapse) للشفاء
- Multibacillary: For 1-2 Ys & Follow (observe) For 5 Ys.

NB USA Recommendation: (80)

1. Paucibacillary: Dapsone & Rifamp. daily for 1 y.
2. Multibacillary: Daily < Dap. Rif. Lamp. for 2 Ys.
3. No Recommendation for paucib. (single lesion) → Most Cases Resolve

- **New drug therapy:** aim of the use of these drugs:
  1. to over come the problem of Resistance.
  2. To Improve the patient compliance to (MDT) Multi drug therapy.

• Isoprodian: contain mix of:

tab =
- Dapsone (50mg)
- INH (175mg) ✓
- prothionamide (125mg)

very effective

- Dose:
  - 15-30 Kg : 1 tab/d
  - 30-50 Kg : 2 tab/d
  - >50 Kg : 3 tab/d.

• Minocycline "يفيد"

- Very effective in dose of 100mg/d For 3ms
- has bactericidal effect of all M. leprae

• Fluoroquinolones:

(Pe 80/floxacin)
400mg/d For 1-2 ms.
↓
Killing of M. leprae (99.99%) in multi-bacillary patients.

• Clarithromycin:

500mg/d.

2. Immunotherapy:

- IV peripheral blood Lymphocytes.
- IV Transfer factor
- Id Heat Killed "M. lepra Vaccine".

N.B

Child Contact c L.L	• Other lines of ttt
Dapsone 25-75 mg/d every week. or Acidopasone inj/3ms For 3ys.	(1). prevention & Control (2). Patient Education (نوعية المريض بالمرض بالرعاية والعلاج) (3). N Rehabilitation e.g physio therapy (for) paralysis. (4). ttt of Complicated N. damage.

(الجزء ده مهم جدا في Reaction)

(تفاصيلها) **Thalidomide** (2017)

- **Mechanism** (3)

(1) Immunomodulating & Antinflammatory:

- Anti-TNFα. (مهمة جداً..)
- ↓CMI: -- Thelper, -- IFNγ, -- IL12
- ↑HI: ++ IL4, IL5 (B cell activates)
- ↑ Treg.
- Anti-Neutrophil (PG زي كورتيزون)
- Others: Anti- → histamines / PG / A.Choline.

(2) Hypnosedative effect: pass BBB.

(3) Neural & Vascular Tissue effects → Antiangiogenic / Anti Neurogenic (So → PN)

So → Teratogenic / used in Cancer → Antiangiogenic

- **Absorpt**
  - مالوش علاقة بالأكل.
  - peak plasma. (2-6 hrs)

- **Excretion**
  - unknown.
  - Non-Renal
  - half life: 9 hrs.

No
- Relate to food
- Renal Exc
- CYP450 metab.

SE (إرجع تاني للميكانيزم)

(1) Teratogenicity:
- d.t Anti → Angiogenesis / Neurogenesis..
- 100 % specially at (21-36 ...)
- Phocomelia c limb defects → (Absent or under-developm.) &
- عشان كده → ♀: 2 Methods of Contraception قبل العلاج بشهر... / ♂: يلبس Condom + ... وسائل
- هيبقى جزء ... الحمل

STEPS program of: System for Thalidomide Education & prescribing Safety
(1) Consent
(2) Educat packets.
(3) Monitorings.

- pregn. (X)
- Lactat: No

- وسيلة حمل قبله بشهر - اختبار قبله بيوم
- اختبار كل اسبوع لمدة شهر ثم كل شهر.

(2) **P.N** (20-50%) → mild proximal ms. weakness + PP paraesthesia & Anaesthesia.

لسان كده باستمرار الازم عمل قبل وأثناء العلاج:

. **SNAP**: Sensory Nerve Act⁻ Potential.

(3) **Sedat⁻**: & drowsiness

عشان كده باخده بالليل

وزود الجرعة تدريجيا

(Most Common S.E)

(4) **Others**: drowsiness, Xerostomia, Moode changes, ↑ Appetite, Brittle Nails, Edema & Xerosis.

. Thrombocytopenia
. leukopenia
. Erythroderma
. Thrombosis ↙

لما يا خدها
أي دواء آخر...
(Cs or chemo)

C.I

• **Absolute**
. Hypersensitivity
.. pregnancy ⟨ ♂ / ♀ & lactat⁻
. preexisting PN.

• **Relative**
. Hepatic & renal Impairm.
. HTN
. HF
. Hypothyroidism..
. History of ⟨ Neurological disorders. / Thrombosis.

Interact⁻

(1). **Not** metabolized by CYP450 Isoform; So interactions of Importance are those with Additive Sedat⁻ (Alcohol, Barbiturat, chlorpromazine)

(2) **OCP** في الحالات اللي بتاخد من الادوية اللي بيتأثر بيها ستواخدها..

(3) **PN** inducing other drugs.

Indicat⁻ & Dose.

(1). **FDA** → ENL (100-400mg/d)

(2). **Other Responsive (Non FDA):**
. Nodular & Actinic prurigo (because ⟨ .. Neurogenic / sedat⁻ ← ليه فعال)
. PG
. DLE, SCLE, SLE (upto 90% Response) (50-100)

Follow-up.

(1). **أساسي** ⟨ **Pregnancy** . (1) حمل قبل العلاج بشهر (2) إختبار حمل قبل العلاج بيوم ثم كل أسبوع لمدة شهر ثم كل شهر. / **PN** ↓ "SNAP" قبل وأثناء العلاج

(2) **Nerve.** ٣ ثم كل ٦ شهور . تعمل ل ". SNAP"
. Neurological **Exam.**

(3) **CBC** ⟨ leukopenia / ↓ Thrombocytopenia

CLOFAZIMINE

Drug properties: riminophenazine dye (red color)

Mechanism of action:(Antibacterial: Bacteriostatic and slow bactericidal & Antiinflammatory):
1- Disrupts cell membranes (activation of phospholipase A_2 leads to generation of membrane-destabilizing lysophospholipids);
2- Enhances superoxide production;
3- Inhibits neutrophil motility and lymphocyte proliferation

Dermatologic indications: treatment of multibacillary leprosy, other infections (mycobacterial, malacoplakia, rhinoscleroma) and inflammatory skin diseases including neutrophilic dermatoses (pyoderma gangrenosum, granuloma faciale, orofacial granulomatosis, erythema dyschromicum perstans and discoid LE

Dosage: 50–400 mg orally daily[*]; avoid long-term administration of >200 mg daily; (...اكتب طريقته وجرعته في leprosy).
In children:
- Should be given with food or with milk.

Side effects:
1- Discoloration of: skin (red to red–brown diffusely, bluish to violet–brown in lesional sites), hair occurs in 75-100% of and...cornea/conjunctiva and body fluids (urine, sweat, tears); It is reversible but may take several months to disappear after the end of treatment.
2-Xerosis and/ichthyosis;
3- GIT (abdominal pain, nausea, vomiting, diarrhea...the dosage should be reduced or the medication taken less often. Failure to do this may result in accumulation of clofazimine in tissues that can lead to blockage of the intestines..);
4-Ocular irritation;
5-Elevated Liver enzymes;
6-Cardiac arrhythmias (rarely; associated with electrolyte disturbances).

7- Side effects that occur rarely include:

- Dimness of vision: care required if driving or operating machinery.
- Dry, irritated eyes.
- Photosensitivity.
- Weight loss and loss of apetite.
- Depression, which may be due to skin discolouration.

Contraindications: prior hypersensitivity reaction

Pregnancy and lactation: should be avoided during pregnancy (category C, crosses the placenta, and skin discolouration has been seen in neonates.) and lactation (concentrated in breast milk)

د/ مهال اسكام — Dapsone — 2017 — (55)

Syn. → diamino-diphenyl sulfone

Mechanism of Action:

A. Antibacterial → -- dihydrofolic acid of the Bact. → stop its growth.
   - static
   - cidal

B. Anti-inflammatory: → -- Neutrophil Chemotaxis
   (so 1st of choice in Neutrophilic dermatoses).

Preparation:

1. oral Tabs → 50 mg
2. Topical gel → (under trial).

Uses:

A. FDA approved
   - leprosy
   - DH
   - prevention of Pneumocystis Carinii pn. in HIV pt.

B. Non FDA approved: (Neutrophilic dis):

"Bullous":
- Pemphigus family → IgA Pemph.
- Pemphigoid " → (CP, DH, LAD, EBA, BSLE)

"ED":
- PG
- Behcet
- sweet
- Pust. Ps
- GA
- Vasculitis < LCV / EED
- AV

Nodulo-cystic Acne. ← (AV)

Pharmacodynamics:

- Slow but Complete Abs. after oral intake
- widely distributed Except the Eye.
- Skin level is 10 times Serum level.
- doesn't cross the placenta but Excreted in milk.
- Metabolized by liver & Excreted in bile (1%)

SIDE EFFECTS OF DAPSONE

Red blood cell toxicity	• Hemolytic anemia • Methemoglobinemia
White blood cell toxicity	• Leukopenia • Agranulocytosis
Dapsone hypersensitivity syndrome (2-7 ws)	Hepatitis, lymphadenopathy, fatigue, anorexia, Erythroderma.
Cutaneous reactions	• Morbilliform eruption • Urticaria • Fixed drug eruption • Erythema nodosum • Exfoliative dermatitis • Stevens-Johnson syndrome • Toxic epidermal necrolysis • Phototoxicity • Drug-induced lupus erythematosus
Gastrointestinal manifestations*	• Anorexia, nausea • Hepatitis • Cholestatic jaundice • Severe hypoalbuminemia
Neurologic associations*	• Headache, dizziness • Peripheral neuropathy • Blurred vision, tinnitus • Irritability • Psychosis

Dapsone Synd (6th w Synd) = IMN like

P.N

57

NB S.E on Blood — 2 RBCs / 2 WBCs.

Hemolytic Anemia

ستحصل مع كل المرضى الذين يتناولونه (d.t oxidizing effects of sulfones) → ↓ Reduced Glutathion.

دائماً

F.
- G6PD efficient → Compensate
- G6PD deficient → Can't ~

↓

So G6PD assessment

Both → Quantitative & Qualitative.

(أفكار خطط Comprehensive.)

Met hemoglobinemia

Fe^{++} (Ferrous) in Hb

↓ oxidized to

Fe^{+++} (Ferric)

↓

Met Hb → Cyanosis, Breathless, angina.

(Can't → carry O2 or delivery O2 To tissues)

↓

تحصل مع كل المرضى بتكلم دائماً بنسبة [٥ - ١٠٪] دمنيش

Cardio pulmonary manifs

↓

"No Problems"

leucopenia & Agranulocytosis

↓ (< 2000)

may be manifested by:

1. Fever
2. Sore throat
3. Signs of Inf.

↓ So

Stop Dapsone.

NB: Agranulocytosis incid. ↑↑ in:

1. Elderly > 60
2. OH > leprosy (30 times)

How to avoid the Risk of Hemolysis.

(٤ طرق)

- dosing: 100 mg tab & vit E (مهم)
- Pre tt assessment of G6PD (الأهم) → Quantitative, Qualitative.
- Reticulocyte Count assessment (باستمرار أثناء العلاج)
- Dapsone test (مهم): نعطي المريض قرص ونقول له مصل:
  - مشكوبيا أو زرقان
  - في أظافيف ولاها ز
  - احمرار في البول

  وقف العلاج.

Pre ℞ & during ℞ Follow up.

③ قبل العلاج

1. G6PD
2. LFTs
3. RFTs

NB البعض بيقيس:

Met Hb Reductase
to avoid
Met Hb.

③ أثناء العلاج

* كل أسبوع لمدة شهر
كل شهر لمدة 6 شهور
كل 6 شهور " سنة

1. CBC → Reticulocytic Count / Agranulocytosis
2. LFTs
3. Neurological Exam

كهرباء: ① تنميل
Manual Tasks
② تقليل عشى طرفين صوابعهم

Any disturbance → Stop ℞.

Drug interaction:

- Probencid → ↓ renal Exc.
- Rifampacin → ↓ serum halflife.
- phenacetin → ↑ RBCs toxicity
- PABA → Interfer c̄ Dapsone Act°.
  ↓ اسمها زي الأول فاهرس مجرة vit B
- Methotrexate: (اديه العلاج بيهما)

مشهور: Antidote of Dapsone Toxicity is IV Methylene Blue

Contra indications:

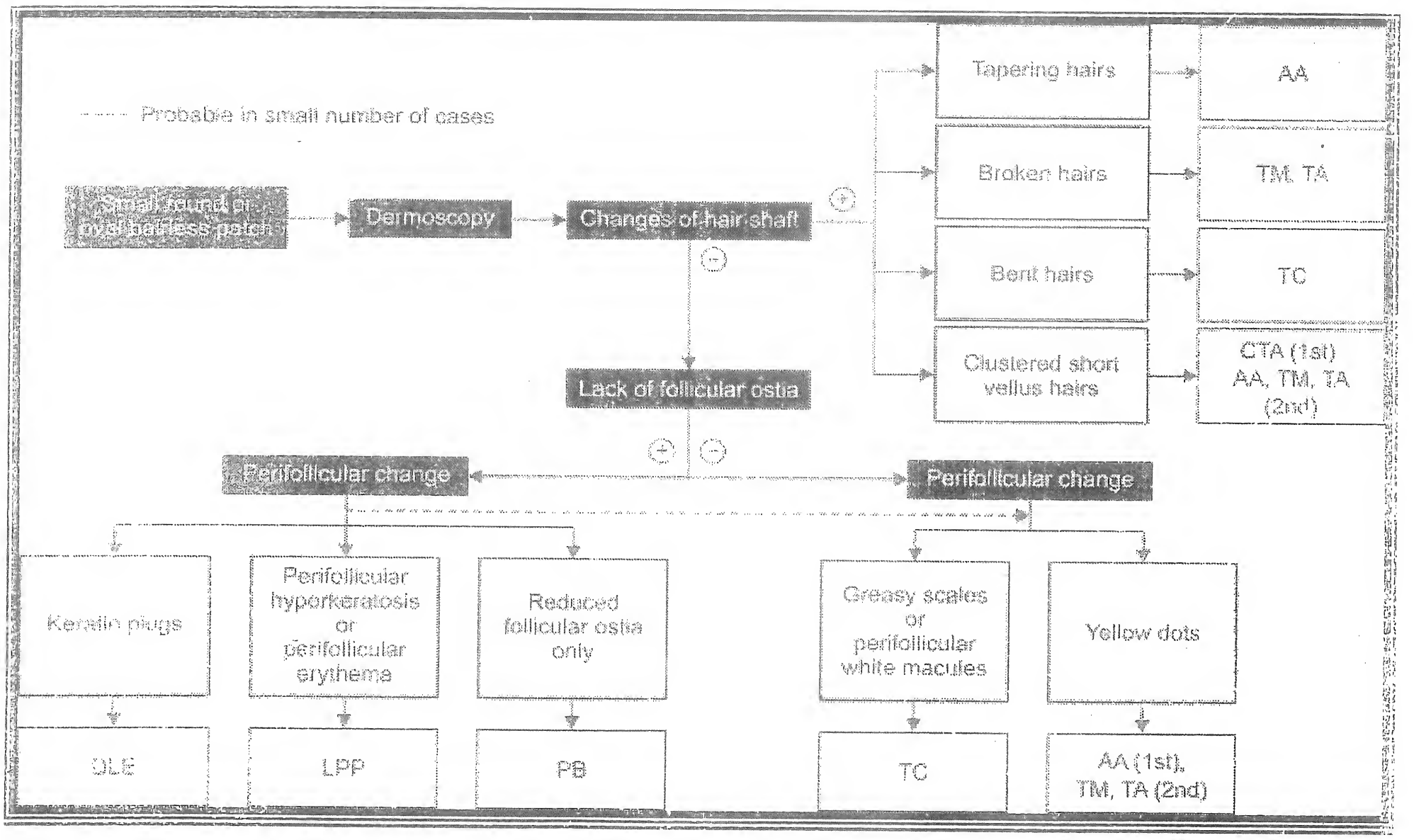
- deficient < G6PD & / Met Hb
- LFTs & RFTs Impairment
- Anemia & leukopenia
- Lactat° (Excreted in Milk. Some reports recorded Hemolytic anemia in fetus but Am. AC of Ped approved it when indicated).
- Hypersensitivity

Pregnancy: → Category C [Can be given in leprosy]

Dermoscopy of Hair Disorders

AGA	AA	Trichotillomania	LPP	DLE	Hair shaft disorders	Telogen effluvium	Tinea capitis
Hair shaft diameter variation of>20% hair shaft (earliest feature)	Yellow dots with short vellus, dystrophic and tapered hairs	Hair shafts of variable length	Perifilar casts	Atrophy	Monilethrix (beaded shaft)	Diagnosis of exclusion	Black dot tinea shows stubs of broken hair shafts with scaling
Perifilar halo in early stages	Black dots (cadaverized broken hairs)	Longitudinal splitting of hair shafts	Target pattern "blue-grey dots"	Complete follicular paucity	Trichorrhexis nodosa (brush fractures)	Decreased hair density with presence of empty follicles over the entire scalp area with no site predilection	Comma shaped stubs are a specific feature
Predominance of follicles bearing single hair	Trichogram shows dystrophic fractured and telogen roots	Coiled fractured hair shafts	Spared intervening follicles	Arborizing telengiectasia	Trichorrhexis invaginata (shaft nodes)		Blotchy pigmentation, erythema, scaling, pustules and follicular scale-crust formation are seen in inflammatory tinea capitis
Hypertrophy of sebaceous glands	Trichogram shows anagen roots White dots	Hyperkeratotic follicular scales	Pilitorti (twisted shafts)				

AGA - Androgenetic alopecia, AA – Alopecia areata, LPP – Lichen planopilaris, DLE – Discoid lupus erythematosus



(عشقتني ع الأشكال)

DH (Dermatitis Herpetiformis) (45)

(Duhring dis)

- Associations:

I Common:

1. Gluten sensitivity enteropathy (GSE): Celiac dis (CD) (100%)
2. Hashimoto Thyroiditis
3. DM (Insulin dependent)
4. Intestinal lymphoma

II Rare:

- Addison
- Alopecia
- AICTDs
- Sarcoidosis

Celiac disease (CD)

- Def. chr. GIT dis. ch by inability to Tolerate Gluten (GSE)
  (its active fact: gliadin ; ⓦ present in: Wheat, rye & barely)
- Intestinal mucosa: 3 grades of affect:
  1. just infiltrat of Lamina propria by lymphocytes
  2. mild villus atrophy
  3. " " "

---

① كل حالات الـ DH معاها CD دكتم فقط ٢٠٪ من حالات CD معاها DH
② ليه الـ CD بيظهر ع الاطفال أعراضه بينما أعراض DH ع الكبار ؟؟ تكوين IgA وتأثيره عايز بيأخذ فترة
③ ليه كتير من الحالات مش معاها أعراض CD (No Abdominal Symptoms) ؟؟ لانه معظم بيكون تأثير الامعاء Mild

---

C/P (No mucosal affect)

Adulthood DH

- Eruption:
  - Polymorphic: Papules, Vesicles < Bullae ∓, urticarial or Targetoid lesions.
  - grouping (ar)
  - Bilat., Symm. on extensors:
    - limbs.
    - shoulders.
    - buttocks.
    - postaxillary Folds.
  - Severely itchy (paroxysmal)
  - Healing: scarring & pigm.
- Flaring: usually ē ingestion of Gluten or Iodide containing food.
- Abdom. manifs: ± Pain or diarrhea, undernourishment.

Childhood DH

↓

as in adults + Palmar blisters or Brown macules.

NB

the clue finding is Spont Remission that lasting as long as 1w that terminating abruptly ē New Crops.

Pathogenesis of DH

- Interaction bet 3:

1. Genetics (أهم) — HLA DQ2 (90٪) / HLA DQ8 (10٪)
2. Environmental factors: Gluten & Iodides
3. Autoimmunity: IgA autoabs.

- Gluten: Containing diet e.g Wheats → Passes to lamina propria of The Intestine.

e. GT_2

↓

Gliadin-TG2 complex

↓

Formation of Anti-TG2 IgA autoantibodies

↓

Cross react with Epidermal TG3

↓

Formation of IgA-TG3 Immun-complexes

↓

deposition in dermal papillae (with Neutrophil chemotaxis.

- Subepid. blisters (L.L)
- Neutrophil Microabscesses (IgA → ++ C3a → ++ Neut.).
- granular IgA deposit at dermal Papillae. (NOT BMZ as in LAD)

- Dapsone: ↓ Neutrophil accumulation
- Iodides: ++ ↓ ↓

- even if Topical Iodide Test To confirm Ø

Dapsone is ++ of dis. of Neutrophils or IgA.

Gliadin: is frachim of Gluten

TGs: enzymes, Tissues (TG2) & Gliadin as substrates

((N B))

يعني
سنتيه دابسون
حم رقص GFD،
الدابسون ويكمل
GFD

. GFD = Gluten . free diet

Dapsone نقلل تكيبه نتيجة مارن
بيننتبح إ تنا وم

. Sulfasalazine: Category (B) in pregnancy.

. Dose : 1 - 2 gm/d
. Sulfapyridine : gm/d.

. S.C . Hypersensitivity.
. Hemolytic anemia
. Proteinuria
. Nusea & Vomiting الاوقد

لازم شرب كيه ماد كبيرة

. Sulphapyridines:

. Sulphasalazine 1 - 2 gm/d
. Sulphapyridine 2 - 6 gm.
. Sulfamethoxypyridazine 0.5 - 1.5 gm/d.

. **Path:** → Subepid (intra L.L) blisters ē Neutrophilic Infilt.
→ Neutrophil microabscesses (in) dermal papillae.

Eos. infilt is +ve So difficult to diff from BP. ?? ↓ do (DIF)

اهم طريقة للتشخيص . **DIF:** → 90 % (granular) IgA in "Dermal papapillae"

hallmark "مهم جداً"

(HL). NB : Granular + lineare (?-10%) . Fibrillar : rare.

. **IIF:** → usually -ve (because IgA formed locally in skin)

. **Circulating Abs:** Anti TG2 (Endomysial), Anti TG3, Antigliadin & Anti-Reticul.

. **Targeted Ag:** → Transglutaminase → Tissue : TG2 ; → Epid = TG3

---

(44)

Stop gluten & Iodine (Atkins diet)
- كُل : O R C (oats, Rice, Corn) الشوفان، ذرة
- لا تأكل : Wheat, & Rye القمح، الشعير
- Value :
  1. ↓ cut & intest. manif.
  2. ↓ Dapsone or (Stop it)
  3. ↓ incid of Lymphoma.

↓ give

Dapsone or SulFapyridine

Dapsone (أكثر شيوعاً):
1. 100-200 mg/d (± ↑ upto 400/day) (أكثر تسبباً في Hemolysis)
2. dramatic Response ē in 48 hrs. ← استخدامه Therapeutic Test
3. For 3-6 ms.

Sulfapyridine:
2-4 gm/d
. Sulfasalazine 1.5-4 gm/d (عكس) $\xrightarrow[\text{To}]{\text{metabolized}}$ Sulfapyridine.

لو لم يفش الدابسون و Sulfapy. → Colchicine, Tetracycline, Nicotinamide, Ciclosporin (but ± → intest. Lymphoma), Heparin

. Cs → Systemic : No effect
→ Topical : ± ↓ itching

الأكلات

• Gluten Containing:

- قمح (الجنز)
- شعير . barley
- جودار (نوع من القمح) . Rye
- المكرونة والسباجتي
- الصلصات عامة وطحان
- القهوة وأنواع السريع
- الآيس كريمي

• Gluten Free:

- الرز
- الذرة
- القهوة الطبيعية
- البطاطس
- الفول الصويا
- الخضروات والفاكهة الطازجة
- الزبادي
- الملح والفلفل
- الجبن الريش
- الشيكولاتة

• Avoid Iodine Containing Food:

- Iodized Salt
- Fish & Shellfish.

Diagnosis of DH

1. Hpg: DIF & IIF
2. Genetic: HLA → DQ2 / DQ8
3. Intestinal Biopsy
4. Iodine & Dapsone Test.
5. Investigate for Associations.

بعض المصطلحات:

- IIF → -ve because IgA Formed Locally & dont circulate
- endomysium: CT that ensheaths the ms fiber.

LAD = linear IgA Dermatosis (LABD = linear IgA Bullous D)

. has 2 Age Peaks :

(1) Childhood Type : . Called Chronic Bullous dis. of childhood (CBDC)

. onset < 5 y.s , Resolut after 3-6 y.s

(2) Adult Type : ~ 60 y.s.

CIP : . Itchy
. Vesicles & Bullae — Clear or Hgic
. on — NL Erythematous or urticarial → Skin

. Pattern : 1 "String of pearls / Beads" : Vesicles & Bullae are at the edge of Annular or Polycyclic Erythematous or urticarial plaques.

2 Discrete : BP like
3 Grouped : DH like. → More ē Adult Type.

. Distribut :

1. Childhood Type : (Flexural)
. lower abdomen , Anogenital & Perineum
. Acrofacial & Pericoral.

2. Adult Type : Trunk & L.L

4 other Non classical lesions :
. Erythematous (Macules Papules plaques)
. EM - like (Targetoid)
. Morbilliform.
. Cicatricial Variant : EBA or CP like (ē severe Mucosal affect)

LAD ē children called Chronic Bullous dis. ē childhood (CBDC)

· NB: Skin lesions are itchy & have Burning sensation (but < DH).

MM affect (≃50٪) · Common & ± Early sign.
· has Cp like picture. (Severe).
· Any Mucosal site ± affected.

· Incid:
· 50٪
· Early
· Severe
· Multiple
CP like

· Pathology → Non specific DH or BP like

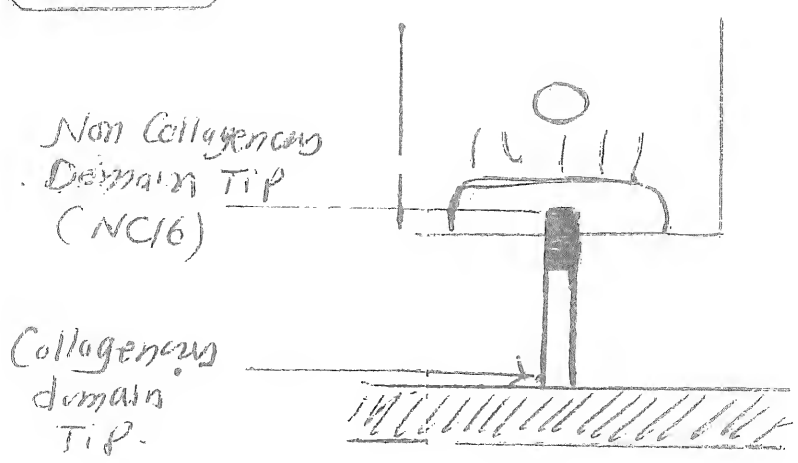
Subepidermal Blisters ē Neutrophilic Infilt. (DH Microabscessed like); ± with Eosinophils (BP like)..

· Path res & DIF

DH:
- granular IgA & Neut. at dermal papillae

LAD: linear IgA & Neut at very tip.

(NB) on BPAg2 / 180 KD / Collagen 17:



· BPAg2 has 2 parts:
① intracellular part → Not Target in Bullous dis.
② Extracellular → Targeted; has 2 parts:
(i) NCW1: أول جزء بيظهر خارج الخلية ويكون ناحية "NC16 tip"
(ii) LABD97: Collagenous أو LD ناحية domain Tip.

· DIF: · Linear IgA at (Not at D-papillae as in DH).
- L-L (Mainly)
- SLD (ass. ē Anchoring fibrils) (±)

· ± linear C3 & IgG (BP like).

· IIF: ≃ 50٪ IgA antibodies directed against:

(Ag)
- L-L ←
- LD → ladinin.
- SLD -

· L-L antigens: [· 97 KD · 120 KD [Portions of Extra-cellular domain of BPA92] · 285 KD [Ag in L-L] (LAD 285)]
or
· LD: Ladinin
· SLD (minority of cases) → Anti Coll 7 antibs. (Anti-250 KD protein Abs which is part from Coll 7A).

. NB1: Conditions that may associate LABD:

- ulcerative Colitis (70%)
- Malignancy
- Drugs.
- Gluten sensitivity (GSE). (Rare)

NB2 . Types of LABD: (4 Main types):

1. Idiopathic (Classical) Type: 2 Age peaks
   - preschool (5y)
   - 60 ys.
2. Malignant associated Type.
3. Drug induced: (جرعة بدأت)
   - Most Common: Vancomycin. (هام جداً)
   - less Common: ACEI, NSAIDs, penicillin, & Cephalosporins, "diclofenac"
   - uncommon: phenytoin & Sulfa.
   - rare: Ciclosporin, PUVA, Rifamp.

   2 Ch:
   - No MM
   - resolve after stop of drugs by 2-6 ws.
4. GIT disorders. GSE (CD) & U. Colitis. (rare)
5. Autoimmune ass.: AICTDs.

. Prognosis of LABD: in Majority of cases; resolve after 3-6 ys.

← ١٥ سنة كاملة باللي [10-15% in 30-60%]

. Treatment

أهم علاجين

1. Dapsone: (الأهم) → dramatic č in 2-3 ds.
   - children: 1 m/Kg/d
   - Adult: 100-150 m/d.
2. Sulphapyridine: (بديل الدابسون)
   - 1.5 - 3 gm.

. Others:

1. Cs (systemic)
   ممكن تحتاج تضيفها للدابسون
   عشان تغطي نتيجة أفضل
   - usually Needed For pt. č IgA & IgG deposit.
2. others (~ağ) → (empirical)
   - Tetracycline, (dicloxacillin) & Erythromycin
   - other Immunosupp.

سؤال التعالم

	DH	LABD	BP
• HLADQ2	> 90%	30%	20% (NL)
• Enteropathy	> 90%	Rare	No
• lesion skin	Grouped: papules & Vesicles at Extensors	Vesicles or Bullae discrete, grouped or Crown of Jewels. either — DH or BP like	discrete Bullae, Trunk & extremities.
• MM	No	• Severe	• uncommon & mild
• HP	Subepid. bullae ē Neut. infilt.	Subepid bullae ē Neut. infilt. & ± Eosinophil	• Subepid bullae ē Eosinophilic infilt.
• DIF	• Granular IgA at Dermal papillae	• Linear IgA & ± IgG at BMZ	• linear IgG & C3 at BMZ
• IIF	• ± Ve	• See before	• See before
• Dapsone Response	Excellent	Good ± Cs	• weak

(نادر ال) خالص دايوى (A-1)

EBA (Epidermolysis Bullosa Acquisita)

- Any age but usually (40-50 Ys).
- Associated ± :
  - IBD (Specially Crohn's) ← "Most Common"
  - MG → lymphoma
  - AICTDs

C/P: 2 Types

Inflammatory Type (Generalized, Non Scarring)

B.P (Dermolytic P.) or CP like.

↓ wide spread tense bullae → No Scarring

↓ Ht (good prog. / responsive)

1. Cs
2. Dapsone
3. Immune Supp.
4. IVIG

Non. Inflammatory (localized, Scarring) ← More Common (الأشهر)

DEB or PCT like [So Called Acquired Mechanobullous]

↓

- Skin: Traumatic blister → (↑ Fragility) Scar, Hyperpigm. & Milia. (Acral & Trauma Sites) — elbows, knees, dorsal Hand & Feet.
- Hair → Scarring Alopecia.
- Nail → dystrophy
- MM → usually affected.

↓ Ht [prolonged / resistant to Ht]

1. avoid Trauma
2. wound manag.m
3. Ht Ms

HP

↓ Subepid (Sub LD) @ ± L.L Blister.

- Neutrophil → inflamm. type
- non inflamm. type → Absent or Sparse infilt.

DIF

↓ 100% .. linear IgG & ±C3 at SLD & ± L.L

IIF

↓ (50%) Anti Collagen VII IgG Antibodies

Tt of EBA

(very chr. dis & very resistant to Tt)

- No universally accepted Tt d.t lack of studies & rare cases.

Best Tt by some authors: اكرم

- دكتورة Steroid + Dapsone or Sulphonamides.
- بردين Colchicine

Other lines:
- Pulse Cs
- Azath.
- MTX
- Vit. E & C
- Ciclosporin
- IVIG
- Plasmapheresis.

Bullous SLE

خاص دايس — شائعة
- IgG & IgA against Coll 7
- during exacerbation (غالبا)

- **Def.** Transient autoimmune blistering condition that occurs in the setting of SLE (1% of cases)

- **NB:** there is some controversy as to whether the term include all bullous erupt. ē SLE or should be reserved for those ē derma Ag. [Coll 7].

- C/P / Typical criteria for Ø (see CTDs)

- **Histopathology** Lever " 3 Histologic pattern:
  1. DH like → Most common. (Subepid. blistering ē dermal Neut. microabscesses)
  2. Basal cell layer vacuolization ē subsequent blistering
  3. Vasculitis ē subepid blister & pustule formation.

(to diff. from DH:
- Mucin deposition (among collagen)
- Thickening of BMZ.

BSLE

(Photodistributed) ↑ Specially

1. CIP: SLE picture + Generalized blister
2. HP: Subepid blister ē neutrophilic Infil.
   ± DH or LABD like
3. IDIF & IIF: EBA like.
4. Steriod., Dapsone, MTX ~~or~~ Rituximab.

Self limiting ↙

Now! So How to diff.

- **EBA**
  - Trauma s.t
  - Skin fragility
  - Heal ē scarr.
  - IgG only

- **BSLE**
  - sun exposed areas (mainly)
  - Hx & manif ☐ SLE
  - dramatic Resp. (+) dapsone.
  - IgG & IgA.

Imp: 2 diseases ē dramatic Response to Dapsone ?? → DH & BSLE (also LAD)

EBA & B.P (عكس إمتحان)

- Blister → B.P: L-L.
  EBA: SLD.
- infilt → Eosin.
  Neut.
- C3 → : B.P > IgG (which) EBA عكس
- Salt split skin Test (SSST)
  - BP: epid. side.
  - EBA: derm side
- Skin Biopsy & Immunohistoch
  - Collagen 7 Abs < BP: at base of blister
    EBA: " Roof. " "

DIF: EBA → U serrated pattern / BP linear.

- EBA & BSLE → clinic
- BSLE → clinically as → DH or BP
  Immunologically → EBA.

SSST: "Salt split Skin TEST"

(Subepid. اختبار واحد لكل)

Separation of DEJ through (L.L) by factor.. exposure to hyper tonic 1 molar NaCl for 1-2 days at 4°c, (is) essential for IF evaluation of subepid bullous dis.

Nacl 4°c

. Can be done for both DIF & IIF, in the (عملياً) (الأهم)

Later the autoAbs will reacte the epid &/or dermal side of Skin.

Epid.

(anti BP Ag2) →
- BP
- CP
- HG
- LABD (Majority)

- EBA
- BSLE
- BP (anti-P 105)
- CP (antilaminin CP)
- LABD (minority)

. DH

• Dapsone in Subepid. Blistering dis.

- localized CP
- DH
- LABD
- EBA
- BSLE
- SCPD

. Coll 7 Autoimmun bulloss → EBA, BSLE, ± LABD

. Coll 7 Non " " : EBD.

Non Auto Immune Bullous diseases

Subcorneal pustular dermatosis (Sneddon & Wilkinson, 1956)

It is a chronic benign/relapsing/pustular eruption which affects mainly the trunk, spares the face and mucous membranes and histologically shows subcorneal bulla which contains polymorphonuclear leukocytes.

- **Age:** 40 - 50 ys., **Sex:** more in female (4:1).
- **Clinically:** Chronic relapsing disorder, with sterile pustules in annular or serpiginous patterns mainly on the abdomen, axillae, and groins. Pus accumulates in the lower half of large pustule (level). Healing occurs with superficial crust and later on with brown pigmentation. **The face is never affected nor the mucous membranes.**
- **Associations:** IgA monoclonal gammopathy, pyoderma gangrenosum, inf. bowel dis.
- **Histopathologically:** Subcorneal neutrophils. Later, few 2ry acantholytic cells are seen at the base of a pustule (probably due to proteolytic enzymes present in the pustular content). Dilated capillaries and perivascular mainly neutrophilic infiltrate are present in the underlying dermis.

  Some authors believe that subcorneal pustular dermatosis is a variant of pustular psoriasis, however, spongiform pustules occur only in pustular psoriasis.
- **Treatment:** Dapsone 50-150 mg daily or sulfapyridine.

Subcorneal or intracorneal separation with:

Neutrophils predominant	Eosinophils predominant	No or few inflammatory cells
• Impetigo contagiosa	• Erythema toxicum neonatorum	• SSS syndrome
• Pustular psoriasis		• Bullous impetigo
• Subcorneal pust. dermatosis		• Pemphigus fol.
• IgA pemphigus (SPD type)		• Pemphigus erythem.
• Candidiasis	• Eosinoph. pust. folliculitis	• Miliaria crystallina

NB:

SCPD like dis

- pustular PS.
- SCPD like IgA Pemphigus.
- Microbial pustulosis of the folds
- Pyoderma Vegetans.

(1939) ايام ← Hailey - Hailey (HH) (Darier أحوال)

(Familial Benign chronic pemphigus)

Inheritance:

- AD
- +FH → (60%)

- Age: 30-40 ys.
- Pathophysiology: < Genetic + others

- defect on gene called (ATP2C1)
  Chromosome 3q21-24 —Codes For→ protein hSPCA1
  w̄ is Ca+ & Mn. pump → defective
  desmosomes (depend on Ca+) → separation

- Other Factors share in the dis: (5)
  - Heat, Friction, Inf (Bact & Yeast), sweating.
  - UVB: provokes acantholysis (& used to detect Gene Carriers).
  - lithium

- ultrastructural studies: KCs show:
  - retracted tonofilaments
  - Elongated memb. microvilli
  - ↓ No of desmosomes.

DD: Darier:
1. Age
2. Gene & protein
3. site: Flexural (Darier: Seborrhic & Flexural)
4. No hand lesion
5. rare MM
6. Nail: white
7. No: salivary, ocular, Neuro
8 HP
9. HP
10. lesion

C/P: → Flaccid vesiculopustules: < crusted lesions. / circinate " . / vegetating " .
- that rupture → crusted lesions or
- form expanding circinate plaques ē central healing → pigmentation or
- Form moist, malodorous flat soft vegetations ē painful fissures & (2ry Inf.)

Site → Flexures (one site or multiple sites)

- Pain, burning & itching → limit the mobility of Flexures.
- Bad odour

- other ass. cut. lesions: < PP pits, Nail bands (white) —4ĉ→ Darrier.
  Mucosal: (rare) oral (bucc) ± vaginal or Esoph.

[Darier < Nail: Red & white Bands. / MM: Common]

. Complications:
1. Kaposi Varicelli form eruption)
2. ACD
3. Malignant transformation → SCC (تحصل)

. prognosis:
- Exacerbation usually at warm seasons.
- improvement occur in old ages.

. Pathology:
- Dyskeratosis (±)
- Acantholysis: (+++)

Darier: Acantholysis + Dyskeratosis but Dysk. > Acantholysis

→ Suprabasal Acantholysis: partial or less extensive < (PV)
→ Few bridges (desmosomes) remains → Dilapidated brickwall

→ Villi inside the Blister Cavity. (Elongated dermal Papillae) & a single layer of Basal Cells lines the Villi.

. ultrastructure: → dissolution of Desmosomal plaques → KIF separation → aggregation around Nucleus → Dyskeratosis

. IF: → ??

; Treatment [Course Waxes & Wanes].

[1] Topical:
. Soothing Compresses: Alum. Acetate (1:40) dilution; Alum. Chl. 20% in Alcohol
. Topical Cs
. Topical Antib. & Antifungals.
. Diavonex (Control Ca+).

[2]. Systemic:
. Antibiotics (tetracycline & Erythromycin) → – protease Activation
. Cs (-- Acantholysis).
. MTX
. Retinoids (Few reports) +ve Cmed. [X] → [Darier Cure]
. PUVA (±)

[3] Recent
. Botox → ↓ hyperhidrosis.

[4] Grenz Zone Therapy.

[5]. Surgical: dermabrasion + CO_2 laser, Cryo

Genetic Blistering diseases

- Darier
- Hailey- Hailey

Etiopathogenesis مقدمة لمعرفة

- Desmosome عنصر أساسي في تركيب الـ Ca^{+2}.
- مصدر هذا الـ Ca^{+} هو سيتوبلازم الخلية (Cytosol)
- الـ Desmosome كبروتين بيتم تكوينه في عضوين من أعضاء الخلية بالترتيب

مهم للحفظ

[1.] Endoplasmic Reticulum (ER) Then:

[2.] Golgi apparatus

- لكي يتم ضخ الـ Ca^{+} من السيتوبلازم الى داخل
ER
G.A
نحتاج بروتينات هي

(ATP2A2 & SERCA2)

[A] • ER —محتاج البروتين→ SERCA2 (Sarcoendoplasmic Reticulum ATPase 2 protein)

وهذا البروتين المسئول عن تصنيعه هو جين اسمه

[ATP2A2] Gene.

(ATP2C1 & hSPCA1)

[B]. GA —محتاج البروتين→ hSPCA1 (Human Secretory Pathway Ca^{+}/Mn^{+} ATPase -1) protein

وهذا البروتين المسئول عن تصنيعه هو جين

[ATP2C1] اسمه

(يعني)

[1.] Gene: ATP2A2 —encodes→ hSERCA2 protein → Pumps Ca^{+2} from Cytoplasm to ER

[2.] Gene: ATP2C1 —encodes→ hSPCA1 protein → Ca^{+} pumping To Golgi

---

• So Genetic Mutation in Any of The 2 Genes:

(1) Defective Desmosome → Acantholysis

(2) protein Accumulation inside ER & Golgi → Apoptosis or Dyskeratosis.

Darier Disease

(Keratosis / Dyskeratosis Follicularis)

- **Etiopathogenesis**: **AD Genetic** + **Enviromental**
  - AD Genetic → Mutat. in ATP2A2 gene on chromosome 12q24 → defective $SERCA_2$ protein → Failed Ca^+ pump in ER → Acanthylosis & Dyskeratosis
  - Enviromental →
    - Heat
    - Frict.
    - Infect.
    - UVB
    - Lithium
    - Premenostrual

- **Epidemiology**:
  - **Age**: 6-20 Ys, M = F.
  - **Course**: Exacerbat. ([illegible]) & Remission.

C/P

Skin

(1) dirty, crusted, keratotic, red-brown papules at seborrhea sites:
- Face
- Marginal scalp [Postauricular] ([illegible])
- Lat. neck & upper trunk
- **Flexures** (DD H-H)

- Coalescence of lesions → Macerated & papillomatous plaques → **Bad odour** ([illegible])

(2) **Guttate leukoderma**: in dark skin individuals.

(3) **Hands**
- **Dorsal**: plane wart like lesions; **also** feet, legs & arms.
- **Palmar**: Keratotic pits & papules.

MM (15-50%)

- Whitish papules specially at palate.

Nail ([illegible])

1. Longitudinal white, red or alternating white & red lines (**SanWitch Nail**)
2. Distal V-shapped nicks / notches
3. Longitudinal ridging, fissuring & brittling.

[illegible]

- Seborrheic
- Flexural
- Hands
- Nails
- MM

Nail
- Leukonychia
- Erythronychia
- V-Nicks

- **Systemic Manifs**: Salivary, ocular & neuropsychiatric complications.

- Clinical Varieties:

[1] Segmental Darier: along Blashko lines.

[2] Acral Hemorrhagic: Hge into acantholytic vesicles; red - blue black macules at palms & soles also dorsal aspects.

(Solitary Darier) → [3] Warty Dyskeratoma.

- Complication of Darier:

تكلي تخرفض بيرض خواي تنفسي سيئة → [1.] Malodour, Pain, itching & burning sensat°

[2.] Kaposi - Varicelliform Erupt°: (See viral)
عدله ناية عداله ناية مراكز في حالات
[Local infect°] حالات KVE ذلك نتيجه
of disturbed skin barrier

[3] Salivary gland obst. → Painful swelling

[4] Ocular: ulcerat° & Inf.

[5] Neuropsychiatric Changes: — Epilepsy, mood changes, intellectual impairment.

[6] SCC (Cut - & oral)

- Histopathology: Acantholytic Dyskeratosis
= Acantholysis + Dyskeratosis (2 Types of Dyskeratotic Cells).

Acantholysis → Suprabasal ē Eosinophilic Infilt. (أزرار فقاعي) bullous ē

Corps Ronds	Grains
. at lower epid (spinous layer)	. upper epid. (St. Corneum)
. large Cell (KCs)	. Small Cell
. Darkly Stained, partially Fragmented Nucleus Surrounded by Clear Cytoplasm & encircled by bright ring of Collapsed Keratin.	. Shrunken nucleus
	. Intense Eosinophilic Cytoplasm.

DD

[A] Clinically

(i) Flexural lesions — P. Vegetans, Pemphigoid Vegetans, Pyoderma Vegetans, H-H. (3 Vegetans)

(2) Dorsal Hand lesion (Plane wart like lesion,)

(i) Acrokeratosis Verruciformis of Hopf

Forme Fruste (Incomplete Type of Darier) — بعض يعتبره

- AD
- ATP2A2 gene mutation
- dorsal Hand lesions ± Nails
- No — Acantholysis Nor Dyskeratosis.

(ii) EDV

(3) Truncal lesion: Grover (TAD)

[B] Histopathelogically: Acantholytic Dyskeratotic Dermatoses.

(i) Darier
(ii) H-H
(iii) Grover
(IV) Warty Dyskeratoma (Solitary Darier) — طلعولنا
(V) linear Acantholytic Dyskeratotic epid. Nevi

Treatment

(1) General: Cotton clothes, sunscreens, ↓ fricn & moisture,
- Antibiotic & Antifungal cleansers (↓ odour)
- Keratolytic & Emollients.

(2) Topical: Cs, 5FU & Retinoids.

(3) Acitretin & Isotretinoin: Very effective (Except in predominant bullous or Intertrigenous lesions → Aggravate)

(4) Ciclosporin: if Failed Retinoids.

(5) dCPs: in Premenestrual Flare

(6) Surgical, Laser — Erbium, Co2: To remove The plagues Vegetating.

Histo—logy

Cell size will
Nucleus large

. MCs :

. An & epid. | Nevus :

. CRP

. Skin Pags

% Rat ...

. Mouse

. MR : 10 - 20

Mnemonic

ID Scalp : Cause of
Thal.

Most Common Cause

. Idiopathic

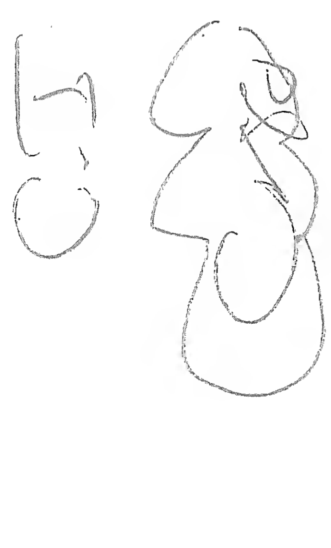
AGA < AD / PJ

Scales

Fine | Bran like | Sheet like

. AD
. Fungal

SD



. Blood Culture

Clp: . The medial Ankle is most frequent & severly involved area (because it represent a watter shed area with relatively poor lymphatic flow compared with rest of the leg); with advancement of the dis → encircling of ankle, Below Knee Extension (Stocking Erythroderma) & ± dorsal foot.

Site

lesion

. Reddish-Brown discoloration is the Earliest sign.

. There are Severe acute inflammatory, oozing Patches & plaques that may be ass. with:
Honey-colored crusting (d/t bact.) or Monomorphous pustules (d/t cut. Candidiasis).

. Long Standing lesions may show:

1. Hyperpigm.
2. Lichenification ?? (Hemosiderin deposits)
3. Lipodermatosclerosis (Dermal Fibrosis with inverted Champagne bottle appearance)
4. Pseudokaposi Sarcoma or Acroangiodermatitis:
   . Unique feature may be seen in stasis D/S by Violaceous Nodules & plaque on dorsal feet that may undergo painful ulcerate Simulating a Kaposi Sarcoma"

x . Skin may show other venous insufficiency changes:

. Edema
. Varicosities
. Atrophie blanche
. Hyperpigm. (d/t Hemosiderosis)

. Investigations:

1. Doppler studies → diagnose of DVT & Valve integrity.
2. Histopath. → Eczema + Hemosiderosis.

Complications:

1. Impetigonization & 2ry bact. inf.
2. Cellulitis.
3. Id reacts.
4. Lichenification.
5. Hyperpigm.
6. lipodermatosclerosis.
7. Atrophie blanche
8. ulcerate (Stasis ulcer)
9. CD (Squamous cell)

(اتى ن) NJBC diff. bet Pseudokaposi & Kaposi:

- Pseudokaposi: Typical Changes of Stasis D. + Capillary & Fibroblas Prolif. → Preexisting
- Kaposi: Vascular Slits + Atypical endothelial Cells + prolif. of Vs independant of The preexisting one.

(اشكر تحل رتيب جرحين دعيف) Treatment (2007)

Compression therapy

1. (شراب السراق) by special Stocking that deliver controlled gradient of pressure.
2. always Leg elevation.

دايما بيبقى رافع رجله ! شكل الطالب أنجض .. (lowest leg Edema) لبس إلشراب قبل إنه ما يتعال بشراب الإنزام:

Assessing pt. arterial Circulat° as if there is impaired circulat° → ↑ Claudicat° & ± ischemic damage.

Medical tt

1. Acute weeping: ECZ → Burow Sol. + Mod. potent CS (oint)
2. Chr. Stasis D. → Calcineurin inhibitors why (No Atrophy & No Tachyphylaxis)
3. tt of inf.: Topical & Systemic Antibiotics
   CD لبعد Neomycin Bacitracin → بالرس
4. Systemic ..., if there is systemic autoeczematizat°
5. long Term: Emollient / under occlusion.

لاحظ: شرط استعمال الـ Cs هنا

1. oint.
2. Mod. Potency (Super potent → (Systemic abs / Atrophy → ulcer))
3. not for long durat°

Surgical tt

1. incompetent Perforators → ligat°
2. Hemosiderosis → IPL (2008)

Recent tt

- Use of drugs that -- Neutrophil Mediated cytokines Release as:
  1. Pentoxifylline
  2. PGE1.

Acroangiodermatitis

(**Synonyms:** pseudo-Kaposi's sarcoma, acroangiodermatitis of Mali-Kuiper, gravitational purpura, stasis purpura)

- **Definition**: was first coined by Mali in 1965. [1] It is a proliferation of *pre-existing vasculature* seen in venous hypertension, arteriovenous malformation, or acquired iatrogenic arteriovenous (AV) fistula.
- Etiopath. : Chr. Venous insuff. → Venous HTN → Tissue Hypoxia → Neovascularization & Fibroblast prolif.
- **C/P:** Confluent, violaceous or brown-black papules cover large areas of the distal parts of the legs. Ulceration and bleeding are sometimes noted. Bilateral lesions are usually associated with chronic venous insufficiency, whereas unilateral lesions suggest an underlying vascular malformation.

- Types :

[1] Mali Type → ass. with Stasis Dermatitis

[2] Stewart-Bluefarb Type → ass. with Congy AV malformation

e.g. Klippel Trenaunay synd

[3] Dermite ocre of Favre : ass. with Pregnancy.

[4] other Types :

(1) AV Fistula of → Shunt in CRF, Stump Dermatitis, in Amputees.

(2) HCV ass. (EMed. 2010).

	Acroangiodermatitis of Mali	Kaposi's sarcoma
• Hp	Small dilated vessels lined by plump endothelial cells with hyperplasia of pre-existing vasculature	Slit-like spaces and spindle cell proliferation. Vascular proliferation is independent of the existing vessels
• PAS	+ ve	- ve
• Factor VIII (& A) in Endoth.	+ ve	- ve
• CD34	Positivity seen on endothelial cells of hyperplastic vessels	Positivity seen on both endothelial cells and the characteristic spindle-shaped, perivascular cells
• RBCs extrav. Hemosiderin (AFB)	Present	Present

Treatment

1- Correction of the underlying chronic venous insufficiency and vascular malformations

2- ***Systemic therapy:*** Various medical modalities of therapy have been tried with favorable results but options are limited. Oral erythromycin 500 mg four times a day

Dapsone

3- Topical CS

4- Vascular cases.

Dyshidrotic Eczema
(Pompholyx, Vesiculobullous hand eczema)

Def: Dyshidrotic eczema is a recurrent or chronic relapsing form of vesicular palmoplantar dermatitis of unknown etiology. Dyshidrotic eczema also is termed pompholyx, which derives from *cheiropompholyx*, which means "hand and bubble" in Greek.

Etiology and pathophysiology: The etiology of dyshidrotic eczema is unresolved and is believed to be multifactorial. Dyshidrotic eczema is considered a reaction pattern caused by various endogenous conditions and exogenous factors:

* 1. Genetic: → AD familial pattern ± present
  → Pomphdyx gene in Chromosome 15q22.1-3
2. Atopy (50% of cases).
3. dyshidrosis: . Not a cause but associate it in 40% of cases & its tt improves Pomphdyx.
4. Emotional Stress.
5. CD (Nickel or Cobalt in diet).
6. Septic focus e.g Strept or dermatophyte.
* 7. Drugs: . Aspirin, IVIG & PUVA.

. CIP: Acute onset of erupts of Bilat & Symmetrical Deep seated vesicles & Bullae at Palms (Cheiropomphdyx), Soles (Pedopompholyx) or Both. Nail fold may be affected → Nail dystrophy. ass. ē Severe itching & Burning.
. Exacerbat ⇌ Remission is Common (Chronic Vesiculo-Bullous Eczema)
. Unilat. Cases may be d/t CD.
. 3rd Most Common Type of Hand Ecz., usally affect middle aged.

. tt 1. Treat the underlying cause.
2. Vesicular lesion → drying Antiseptic lotion.
3. Chronic ~ → Cs, Emollients & Keratolytic
4. Resistant Cases: . Systemic Cs
. MTX
. Radiation

. DD: Pustular Psoriasis

(12)

Ref. All Sources

Asteatotic Eczema
Eczema craquelé, Xerotic eczema, Chapping

Def. Eczema Characterized by pruritic, dry, cracked, and polygonally fissured skin with irregular scaling . It most commonly occurs on the shins of elderly patients, but it may occur on the hands and the trunk.

Etiology and pathophysiology:

Causes

***Multiple etiologic factors may coexist to cause asteatotic dermatitis, including the following:** *(All are associated with ↓↓lipid content of skin):*
(or water)

- **Aging:** due to ↓↓sebaceous and sweat glands activity and ↓↓ Keratin synthesis.
- **↓↓ humidity and cold:**→ increase the loss of water by convection.
- **Wrong Behaviour** :-Frequent or prolonged bathing in hot water and use of soaps, infrequent use of emollients and use of Degreasing agents (Solvents and Cleansers)
- **Atopy**
- **Ichthyosis**
- **Radiation**
- **Drugs** - Antiandrogen therapy[5] and diuretic therapy
- **malabsorption and Nutritional deficiencies** of essential fatty acids, including linoleic acid and linolenic acid , Zinc deficiency[3]
- **Thyroid disease** - Myxedema and other thyroid diseases with diminished sweat and sebaceous gland activity[4]
- **Neurologic disorders** - Decreased sweating in denervated areas
- **Malignancies** - Malignant lymphoma,[6] gastric adenocarcinoma,[7] glucagonoma, angioimmunoblastic lymphadenopathy,[8] breast cancer, large-cell lung carcinoma, and colorectal carcinoma[9]

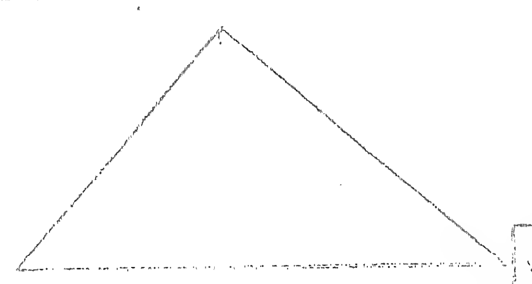
Epidemiology: *Age:elderly>60 y. *Sex:M>F

c/p: Primary lesions: Slightly scaly, inflamed, curvilinearly cracked and/or fissured skin most commonly involves the pretibial areas, but it may also occur on the thighs, on the hands, and on the trunk *(Fitzpatrick likened asteatotic eczema to a dried-up riverbed).*

- Secondary lesions :Excoriated, erythematous, edematous patches may result from rubbing or scratching.

Clinical types: 1-localized: usually pretibial.
2- Generalized (Ichthyosis): ?? Mg

(III)



[1] تعليمات للمريض : الحمام تبعك لازم :
١. لفترة قصيرة (...)
٢. بماء فاتر
٣. بلاش صابون
٤. بلاش صوف
٥. استخدام Humidifier

[2] Emollients:
- استعماله بعد الحمام مباشرة (see AD)
- استعماله دهنيا : 2 مرات على الأقل

• Soaking and Greasing: (Soak & Smear) Technique:
- Soaking: of affected part in Tepid water for 10 min.
- Greasing (Smear): Immediate use of mild Cs oint.
[illegible]

[3] Topical Cs:
- (Mild) Topical Cs (III–VI)
يمكن استعمالها بطريقة ...

(A) Soaking & Greasing (B) under occlusion for 1-2 d

Nummular Eczema

(Discoid Ez.)

Def. Type of Endogenous Ez. ch BY: well defined, Coin-shapped, scaly, plaques usually on arms & legs. ∴ are very itchy & very persistent

- AET & pathophysiology:

"Atopy" (1.) AD (recently considered as adult onset AD)

(2.) Infects (skin usually) colonize or infect it.

(3) Emotional stress.

(4) Xerosis

Clp. Discoid plaques ch BY.

. May undergo central clearing → Annular lesion.

. Very itchy, very chronic

. Usually at: Forearms, legs, Hands, Lumb & Trunk

. Staph. has a Marked Role.

. More in Elderly (60-70s).

Is there a cure for nummular dermatitis?

No. However, the disease can be controlled. Many of the same principles apply here that apply to the treatment of atopic dermatitis. Limiting baths and soap exposure, avoiding irritants, frequent use of emollients, topical corticosteroids, avoiding dry environments, and antihistamines all have a role in treatment. Topical corticosteroids are the mainstay of therapy. With the high rate of staphylococcal colonization, many dermatologists routinely prescribe a 2-week course of oral antibiotics such as dicloxacillin or cephalexin. Systemic steroids should be used only for severe cases and limited to a tapered course over 2–3 weeks. Severe chronic cases may also benefit from PUVA.

Does nummular dermatitis resolve spontaneously?

Yes, but not often. In a prospective study of patients followed for 2 years, 22% were disease-free. Another 25% were free of lesions for weeks to months, but 53% were free of lesions only with continued local therapy. If there is no clearing within 1 year, the disease tends to persist for many years.

(EMal 2009)

Pityriasis Alba

def: Non Specific dermatitis of unknown Aetiology That causes Erythematous Scaly patches → These resolve & leave areas of Hypopigm That slowly repigment to NL.

Aetiology: unknown but ± d.t:

1. ATopy
2. Strept. inf.
3. Sun Exposure (أهم حاجة)
4. ↓ Zinc.
5. ↓ Fe.
6. Parasitic infestations.
7. Malassezia: produces a substance called pityriacitrin → sun filtrate (prevent Natural sun Tanning).

C/P: [1] usually affects dark skin children at summer

[2] has 2 stages:

- Early: ill defined pink erythematous, scaly lesions →
- Late: Hypopigmented (ill defined & scaly)

[3] usually at sun exposed areas

[4] Clinical Varities:

(i) Classical Type: at sun-exposed areas.

(ii) Generalized ~: Bilat & Symm.

(iii) Pigmenting ~, Central bluish pigmented surrounded by ill defined slightly Scaly Halo at the face.

Treatment: (1) Treating The cause e.g Sunscreen, Parasites, vit. deficiency...

(2) Early stage → Hydrocortisone 1%

Late ~ → Emollient

(3) Some Authors: [illegible] Ezallia (Similar [illegible])

صعب جداً وبترجع تاني

Juvenile plantar Dermatosis

(DNNZ)
. Andrew
. Rook

(14)

def. Eczema affecting the feet of Children.

Aet: . Repeated Friction & Macerat^ of feet by: "تكرفتي"

1. occlusive shoes specially Athletic Shoes
2. Abrasive effect of pool surfaces or diving board
3. (Thin) Non-absorbant synthetic stocks.

4 Some consider it manif^ of AD.

. نعتقد أن سببها هو التغير الى حصل في آخر ٣٠ سنة في صناعة الأحذية وشرابات الأطفال (حيث تم استبدال المواد الطبيعية (الصوف، القطن، الجلد) بمواد صناعية (نايلون، بلاستيك) مع تغيير أشكال مساميه من المواد الطبيعية مع الإضافة الى تغطية الأحذية بمواد repellent علشان تحسن الـ durability بتاعة حاجة زي كده.

all these: ↑ Humidity → Feet macerat^ → sweat retent^ → aggravate the condition

لسه في ناس بتقول حاجة لأنه لوحظ في الأطفال اللي بتلبس صنادل وجلد بيحصل برده (So role of friction considered) ✓

CIP: 1 Age: 3 ys – puberty (14).

2 Start as bilat, symmetrical red glazed smooth patches at medial or dorsal aspect of Big Toe → Then spread to involve weight bearing areas of feet as forefoot. (Heel less affected).

Note: Webs & arches are spared.

DD: . AD. . Psoriasis
. CD . Fungal inf.

Treatment: (ممكن تنفع للأطفال على البلوغ)

1. Reduce friction: جزمة جلد – شرابات قطن مناسبة للقدم (porous Foot wear).
2. Emollient.
3. Have rest day: schedule quite time & little or no walking to allow for Healing of fissure
4. Topical Cs.

Hand eczema

تحريري

Hand eczema is such a common and distressing condition, and poses such difficult problems for the dermatologist, that it deserves separate consideration . Up to 30% of occupational medical practice relates to hand eczema, with important issues regarding medical litigation, worker's compensation and disability. One-quarter of the patients referred to a specialized contact dermatitis clinic suffered from hand dermatitis.

Classification: 1-Etiologic classification 2-Morphologic classification
(Rook) 3- Classification Acc. to the Age.

1-Etiologic classification

Exogenous	*Endogenous*
1-ACD: -Delayed hypersensitivity (type IV) (e.g. chromium, rubber) -Immediate hypersensitivity (type I) (e.g. seafood) 2- ICD: -Chemical *(e.g. soap, detergents, solvents)* -Physical *(e.g. friction, minor trauma, cold dry air)* 3-Ingested allergens *(e.g. drugs, possibly nickel, chromium)* 4-Infection *(e.g. following bacterial infection of hand wounds)* 5-Secondary dissemination *(e.g. dermatophytide reaction to tinea pedis)*	1- Atopic 2. Dyshidrotic (Pompholyx) 3. Psychosomatic (↑↑ Eczema > Initiation) 4. Idiopathic (Discoid & Hyperkeratotic Palmar ECZ.).

2-Morphologic classification

1-vesiculobullous hand eczema(Pompholyx) / & patchy vesiculosq.
2-hyperkeratotic hand eczema (Tylotic ECZ.)
3-dry palmer eczema (House wife ECZ)
4-finger tip eczema
5-ring eczema (6. localized thumb ECZ. [illegible])
7-discoid eczema
8-chronic acral dermatitis (Hand ECZ + ↑ IgE)
9-apron eczema ([illegible])
10-gut eczema ([illegible])
11-other patterns (eg.patchy vesiculosquamous)

(4, 5: [illegible])

• Treatment
1. [illegible]
2. Potent or superpotent Cs For 2-3 wk → week-end
3. ± 5 ds / wk → Weak Potent Cs → Tacrolimus.
4. Emollients: [illegible]

تقرّن الشجر

Lichenification

Introduction

Lichenification is a pattern of skin response to repeated scratching or rubbing, characterized *histologically* by acanthosis, hyperkeratosis, and elongated rete ridges, and *clinically* by a thickened skin, with accentuation of the surface makings so that the affected skin surface rese. .les *tree bark*. It may be primary (lichen simplex), without an itchy skin disease and caused by emotional tension, or secondary to an itchy skin disease as venous eczema, atopic dermatitis, chronic contact dermatitis, or chronic infection with T. rubrum of thighs or feet.

Lichen Simplex chronicus (LSC)
(localized Neurodermatitis)

Def. Reaction pattern of skin that arises 2ry to repeated scratching or rubbing [so this not a 1ry process] & ch. by cut. lichenification Δ of:
. Thickening
. Hyperpigm.
. Accentuated skin Markings.

. Etiopathogenesis unknown but ±:
↓
• Emotional stress → Sensation of (burning or) Pruritus → rubbing → lichenification → More rubbing → More lichenific.
(Viscious Circle of itch/scratch cycle)

. Epidemiology: . Age: any but usually 30-50y..
. Sex: ♀ > ♂

. C/P . (1.) itching: . Severe & occurs in Paroxysms of great intensity → tye sorting.
. there is (refractory period) of some hours before until itching recur.

(2.) Skin lesion: . at first: Erythematous, Edematous Excoriated plaques (then) classic picture of lichenification
Lichenified papules ± seen.

* Site : Most Common sites are:

- Occiput
- Nape / Neck → Nuchal area (Lichen Nuchae)] ♀♂
- Perineum & Scrotum (♂)
- Wrist & Ankle
- Extensor forearm.

NB: (i) Giant lichenification of Pautrier
LSC in areas of loose C.T as Genito-Crural area → Solid Tm like plaque & Warty Cribriform surface.

(ii) Notalgia Paresthetica LSC at Bf. tip of Scapula.

- Pathology ⇒ see lichenification

DD (1) lichen amyloidosis (2) L.P (3) Ps.

treatment:

1. Stop Itching (Break the itch/scratch cycle).
   - Anxiolytic
   - مضادات للاكتئاب
2. Cs: Topical & IL.
3. Emollients (2009) (JAAD 2001)
4. Antihistamines, Botox, Topical Aspirin/dichloromethane
5. TENS (Transcut Electric N. Stim).

Other Types of Eczema

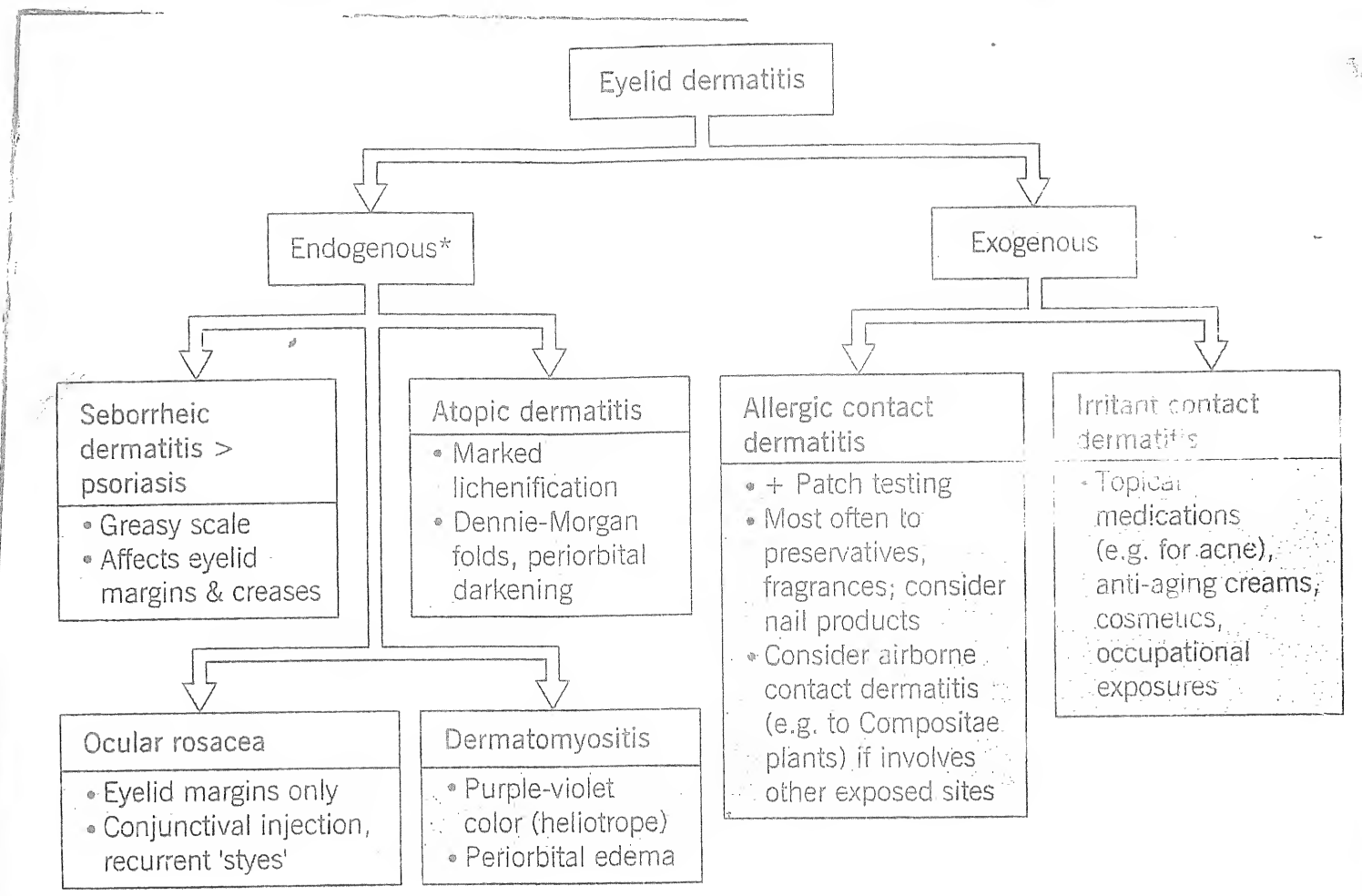
- Frictional lichenoid Dermatitis
- Eye-lid Ecz.
- Breast Ecz.

- **Sandbox or Frictional lichenoid Dermatitis**
  - pin-head sized, white papules at friction sites (Elbows, Knees, Bucky face, Fingers)
  - Etiopath. ?? Friction or Sun.
  - DD: lichen-nitidus.

(NB) In Adults: Dermatitis Papulosa Juvenilis

---

2. Eye-lid Ecz. →



*Diagnostic clues include a history of the condition and characteristic lesions elsewhere

Fig. 13.6 Classification of eyelid dermatitis. More than one etiology may be present, e.g. atopic dermatitis plus irritant contact dermatitis.

---

3. Breast Eczema (Nipple Ecz.)

- ± Affect. Nipple, Areola & Surrounding Skin. (Especially of Nursing Mother).
- Etiology: CD, ND, AD, SD
- Hx: As Ecz. → if No response → (Biopsy) to Exclude "Mammary Paget's"
  - Unilat.
  - Not responding to Cs.

Topical Corticosteriods

Mechanism

1. Antinflammatory
2. Antiproliferative: ↓ DNA synthesis specifically → Lymphocyte & Fibroblast
   → ↓ Collagen → Atrophy
   [all Cs Have These effect except → Hydrocortisone Dermatop
3. Immunosuppressive: — CMI: ↓ IL 2,3,4 5,6 → ↓ T Cell Prolif.
   ↓ IFN-γ
   HI: ↓ Igs product.
4. Vasoconstrict: ↓ → Erythema, Edema, Heat [& ↑ of Hemangioma]

[5. Glucocorticoid Activity
6. Mineralo Corticoid Activity]

NB → Antinflammatory effect is d.t binding to 2 Types of Rs

- CM Rs
  ↓
  CM disrupt
  ↓
  -- phagocytosis & lysosomal release.

- Cytoplasmic Rs

[A] . Cs + Cytosol → enter the nucleus
→ interact ē Nuclear DNA → product of Steriod induced proteins (= Lipocortins)
↓
-- Phospholipase A2
↓
-- Arachidonic acid Formation
↓
↓ synth of → PGs, leukotrienes, PAF.

[B] -- COX enzyme.

• Classification According To Potency

I. European
II. American → Classes

I Superpo
II Potent
III Potent
IV midstren
V midstren
VI mild Po
VII least Potent

احفظ ازى اسمك

• European classification

(كيفظ جيدا عشان الفوارق الجوهرية وشغل السوق)

[1] **Mild potent** (Antinflammatory activity; 1-10)

- Hydrocortisone (Micort)® (Hydrocortisone)®
- Aclomethasone (Perderm)®

[2] **Moderate potent** (Antinflammatory " 10-100)

- Clobetasone butyrate (Eumovate)®
- Hydrocortisone in urea 1%

[3] **Potent** (Activity 100-500)

- Betamethasone — Valerate 0.1% (Betaderm)®
  — dipropionate 0.05% (Diprosone)®
- Mometasone (Elocon)®
- Fluticasone (Cutivate)®
- prednicarbate (Dermatop)®
- Triamcinolone (Kenacort)®

[4] **Superpotent** (> 1500)

- Clobetasol propionate 0.05% (Dermovate)®
- Diflucortolone valerate (Nerisone forte)®

Sideeffects of Topical Cs (20) تيقظوا كويس

جدول مهم.

- Epidermal Atrophy
- Dermal Atrophy
- Steroid addiction Synd
- Skin irritability & Fragility
- Striae
- Purpura
- Telangiectasia (rebound VD)
- Hypo-pigmentat^.

- Hypertrichosis
- Perioral dermatitis
- Periorbital → Cataract / Glaucoma
- Acne vulgaris
- Acne Rosacea
- Exacerbat^ of skin inf. { ↑ incognito / ↓ glu... gra... ulc...
- " " Psoriasis
- Delayed wound healing.

- Systemic absorpt^ → ↑ incid. c̄: 1. Superpotent Cs; 2. children & infant ??; 3. occlusion; 4. wide spread use >50 gm/w supe... or >100 gm/w pote...; 5. Region e.g. delicate skin & Flexures.
  → Commonest HPA supp. (بعد ٣-٤ اسابيع) من استخدام Superpotent ((7.5 gm/d))
- Tachyphylaxis
- Occlusion Complicat^s
- Contact Dermatitis.

Def. ↓ Cs effect c̄ prolonged use
- may occur c̄ in 2w of ttt
- To avoid:
  - Shift to low potent.
  - use on holidays
  - alternative tt e.g. Diavonex; TCI

• Discussion of Complicat^s:

Cs induced Atrophy & effect on skin Layers.

effect on epid.

- epid. thinning occurs after: [1 w of Superpotent; 3 ws of Potent]
- ↓
- thinning; sp. St. Corneum
- ↓
- (1). impair barrier funct^
- (2). ↑ TEWL
- (3). ↑ irritancy & Fragility.

effect on dermis

- ↓ Dermal vol. after 1–3 ws of Superpotent
- d.t
  1. ↓ hyaluronic acid synth. by Fibroblasts
  2. ↑ Water loss
  3. ↓ Collagen synth. & ↓ elastin, ↓ fibroblast
- ↓
  1. dermal Atrophy
  2. Striae
  3. Telangiectasia
  4. Fragility
  5. Purpura (d.t poor vascular support)
  6. ↓ wound healing

استشارات "اوي" — Types

ICD	ACD
1. Frequent 2. ± d.t propylene glycol 3. More c̄ Cream base [تعرض لمستحضرات كريم امين]	less frequent ± caused by: Cs itself / vehicle / preservatives / Fragrances How to suspect: 1. Lack of efficacy 2. Worsening of Lesions

- Patch test help sort out this problem.
- ACD more c̄ Hydrocortisone & Tixocortol & Less c̄ { Clobetasol; Mometasone; Betamethasone }

NB → Skin atrophy may be Reversible 9th step:

. Steroid Addiction Synd:

Mid-high or even Low potent] Cs applied to < Face / Genitals For several Ws → when discontinuing it → Sensat° of < Burning / Severe itching (symptoms of dermatitis that was treated by it in profound manner)

AEt thining of < St. Corneum / Epid → make the patient more susceptable to Irritants

Hlg → discontinue Cs or gradual withdrawal & use of emollients & instruct the pt that symptoms may remains For ws - ms till complete cure.

(As)
- Moisturizers
- Soaps
- Sunscreen
- Make ups.

• Occlusion complications:

1. ↑ incid of systemic Abs.
2. bad odour
3. Miliaria
4. Folliculitis & inject°
5. Reversible atrophy of adjacent skin.

. Indications of Topical Cs

1. dermatitis
2. PLE
3. DLE
4. AA
5. lichen striatus
6. localized pemphigoid
7. كلنر هرا

Contraindications

1. Skin manifs. d.t Vaccinat°
2. Cut. TB & S
3. Skin infect°s
4. Perioral dermatitis
5. Hypersensitivity.

6. Cut- dis not Responsive or Worsened by Cs:

. all C.Is + ← Pit. Rosea, PRP, EM, Urticaria
. Dry skin & Ichthyosis, Large Vs vasculitis, parapsoriasis ← .

. Guidlines For use of Topical Cs

1. Acc. to Potency
2. Acc. To Applicat^
3. Acc. To the vehicle.
4. " " Amount

1. Super potent: ← on small area < 10% BSA, not > 2 wks, not > 50 gm/w, No under occlusion.
2. Potent ← not > 20% BSA, NOT > 3 - 4 wks, NOT > 100 gm/w
± used on Trunk & extremities

(NB) ± used on FaCe For Period < 2 wks ± used in children if failed lower Concs.

3. Mod potent → Tried on hand ecz. & Atopy
4. Mild → used for chr. use in ← FaCe, Flexures, infants & children < 1Y.

2* Acc. to applicat

. Method → ↑ per Cut- Abs. by occlusion.
. Frequency → used in alternate day therapy
. Type of Cs (Tachyphylaxis, ex Cs): when using superpotent: use it 2/day For 2 wks then Rest For 1 w & Repeat For 2 cycles then → either

(1) Shift to lower potency
(2) use on holidays
(3) alternate therapy eg TCI

3. Vehicle: 1. Oint → Chr. dry lichenified lesion
2. Cream → Acute weeping dermatitis
3. Cream, gel, Alcohol lot → hairy areas.

ترتيبهم من حيث القوة.

- Oint
- Emollients
- gels
- Cream
- lot
- Sol.

4. Amount of Cs used:

1. determined by Finger tip Unit (FTU) or is the: amount of cream expressed from a tube of 5 mm diameter from the tip of index to the 1st distal joint. on palmer aspect.

2. 1 FTU = 0.5 gm of medication = will sufficient To treat 2 palm sizes in the average adult.

Site	FTUs
Groin or hand	1
Face or Foot	2
one arm	3
one leg	6
Trunk (front & back)	14

Hidradenitis

(يضاف عليها في شابتر البكتريا)

I-Hurely staging

Table 1. Hurley Classification of Hidradenitis Suppurativa

Hurley Stage	Description
1	Solitary or multiple isolated abscesses without scarring or formation of sinus tracts or fistulas
2	Solitary or multiple widely separated lesions with formation of sinus tracts or fistulas
3	Diffuse or broad involvement of abscesses across a regional area with multiple interconnected sinus tract or fistulas

II- Treatment according to the stage

Hurley Stage	Topical/Intralesional	Systemic	Surgery
Hurley stage I/first-line therapy	Clindamycin Intralesional triamcinolone Resorcinol	Antibiotic Hormonal therapy	Localized surgery
Hurley stage II/second-line therapy		Antibiotic: tetracyclines or clindamycin plus rifampicin	Cold steel excisions CO_2 laser evaporation
Hurley stage III/third-line therapy		Systemic immunosuppressant: dapsone cyclosporine TNF-α inhibitor	Wide excision CO_2 laser evaporation

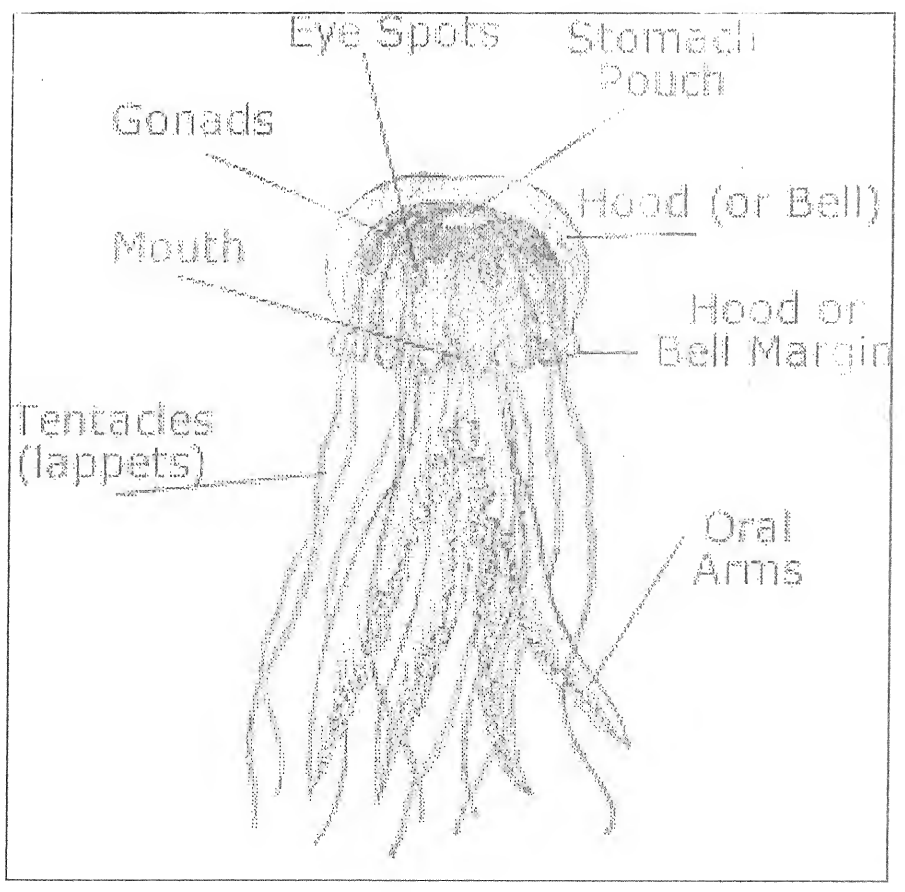
Medscape

Source: Expert Rev Dermatol © 2010 Expert Reviews Ltd

Jellyfish stings

(Eczema.. يضاف علي ورق)

Structurally jellyfish comprise a bell-shaped body with tentacles, some up to 30 metres in length. The nematocysts reside within theses tentacles (مخالب). Stings are delivered when contact is made with the tentacles and nematocysts discharge into the skin.



- Jellyfish are most prevalent in calm warm seawater, sandy beaches and harbours during the summer months. However, they are also seen in other circumstances.

Clinical presentation : The first symptom is of pain, often so severe as to lead to loss of consciousness. Some victims of the some types of jellyfish are unable to make it to the beach alive. Other symptoms include:

- Paraesthesia and itching
- Linear & bizarre shapped Red plaques, patches, & blisters that may become nectotic and eschared.
- Swelling, Sweating in affected area
- Nausea and vomiting
- Muscle pain and cramps.

- Depending on the amount of stinging and the type of jellyfish encountered, shock and cardiac arrest can follow.

-After recovering from the initial sting, the wound may later blister and become necrotic (tissue death).

Treatment:

- Avoid moving the affected limb. Do not rub with a towel or use fresh water as this may cause further damage by causing further nematocyst discharge. Contrary to popular belief urine and alcohol can exacerbate injury and are not recommended.

- Remove nematocysts and tentacles from the skin using gloves and forceps. Razor blades can be used to shave off nematocysts.
- If stung by box jellyfish apply liberal amounts of home vinegar (5% acetic acid (5% acetic acid) will inactivate any undischarged stingers and lessen the severity of the symptoms.), or in its absence, salt water or hot water (40C) for 30 minutes. Seek immediate medical attention.
- If stung by the Portuguese man of war, thoroughly rinse exposed areas with seawater (vinegar is not helpful).
- Ice or an ice pack can help with pain while seeking medical attention.
- Antivenin injections are available in some medical centres for specific jellyfish, and are particularly recommended for box jellyfish stings.
- Topical corticosteroid & antihistamines

Zika virus

- Zika virus is RNA virus of family Flaviviridae that is transmitted by mosquitoe & tick bites in tropical areas and has a prominent cutaneous manifestations.- Zika virus it was first described in humans in the 1960s in Nigeria . cases have bee reported in upper Egypt and transmitted by Aedes Aegypti mosquito. - Only about one in 5 people carrying the virus actually develop symptoms from zika virus infection.

Mode of infection:(-IP: 10 days)

- Mosquito bites: Aedes aegypti mosquitoes breed in and around ponds of stagnant water where humans live and usually bite during daylight hours. When a human is infected the virus circulates the blood for 10 days before symptoms occur. It is during this time that the Aedes mosquito may acquire the virus, then bite and infect another unsuspecting victim.
- Sexually transmitted
- MTC: Through Infected birth canal

-Predisposing factors:

- Overcrowding and poor sanitation
- Poor vector control, e.g., stagnant pools of water for mosquito breeding.
- Travelling to endemic areas

- Clinical features:

- FAHM, fatigue,muscle pain, abdominal pain & vomiting
- Conjunctivitis
- Skin Rash: maculopapular (morbilliform) or scarlatiniform. It starts on the face on the first day of illness and spreads all over the body. It begins to fade within 2–3 days and is gone completely within a week.
- Oral MM: petechiae at mouth and palate.

- Complications

- Guillain-Barré syndrome

- **Birth defects:** The zika virus replicates and persists for several months in the placenta and in the brain tissue of a fetus→GR, fetal loss, microcephaly, brain calcifications &damage

-Diagnosis:

1- Clinical: S&S after Mosquito bites in endemic areas
2- Serology (IgG&IgM): to be repeated after 3 ws if negative

Treatment: The best way to prevent zika virus infections is by preventing spread of the virus by vector control. This means eliminating or controlling mosquito breeding sites. The zika virus-carrying mosquito likes to breed in artificial containers and receptacles containing water in and near buildings.No specific TTT nor vaccine.

Afamelnotide (Melanotan-I)(Scenesse®)

(جديد ..ممكن دكتوراة)

Introduction: α -MSH, production,function & Receptors

1- Pituitary: α -MSH→ ++MC1Rs (Melanocortins Receptors1)→ ↑Eumelanin& ↓ Pheomelanin→ ↓ ↓UVB penetration→ Photoprotection → ↓ ↓incidence of melanoma (Afamelnotide , Melanotan-I)

2-Brain: α -MSH→++MC4&5Rs→Regulation of apetite&sexual function (Bremelanotide ,Melanotan-II)

- **Mechanism of Afamelnotide :** α-MSH analogue,acts non selectively on MC1Rs expressed on melanocytes. It ↑↑ production of eumelanin & ↓↓ Pheomelanin thus provides direct photoprotective& antioxidant effects against harmful UVB radiation.

-**Indications**: Photoprotection for 5 diseases:

- Erythropoietic protoporphyria
- Polymorphous light eruption
- Phototoxicity associated with systemic photodynamic therapy
- Solar urticaria
- Skin cancer: AK&SCC.

- Dosage & Administration

- Afamelanotide (Scenesse®) comes as a white rod approximately 1.7 cm in length and 1.5 mm in diameter.

- It contains 16 mg of afamelanotide and is administered as a subcutaneous implant specially around the hip.

- It is inserted every 2 months, prior to and during summer with a maximum of 4 per year.

- Adverse effects:(Few)

- 30% of patients experience hyperpigmentation at the implant site & darkening of moles anywhere on the body

- Mild tiredness, headache, dizziness and nausea after administration of the implant (usually clears by 72 hours).

- Contraindications (Because no available Data)

- Hepatic and renal impairment,
- Ages before17 and after70 and
- Pregnancy (Women of childbearing potential should use effective contraception during treatment with afamelanotide, and for a period of three months after).

Probiotics and Atopic Dermatitis

(Front Microbiol. 2016)

Briefly, hygiene hypothesis inversely relates the prevalence of allergic diseases and urban lifestyles, high standard sanitary conditions, vaccinations, antibiotic administration, and small family size.

- Probiotics are ingested live microorganisms that, when administered in sufficient amounts, confer health benefits on the host. robiotics contribute to regulating allergic hypersensitivity reactions by suppressing the Th2 mediated response that helps in balancing Th1/ Th2 immune responses and by increasing Treg mediated immune responses

- *Lactobacillus,* Bifidobacteria, and yeasts are *the most frequently studied probiotic strain.*

- probiotic milk administration was done 2–4 weeks prenatally to the pregnant mothers and postnatally to the infants for a 1-year time period

- the prebiotic is a specialized plant fiber that beneficially nourishes the good bacteria already in the large bowel or colon. While probiotics introduce good bacteria into the gut, prebiotics act as a fertilizer for the good bacteria that's already there.

- Probiotics for the prevention or intervention of AD is a vast underestimated area of research; and as a result, there is no reliable evidence to date that strongly supports their safe application. In spite of the weak evidence, a considerable number of clinicians prescribe the use of probiotics for the prevention of eczema. The regular instillation of probiotics in daily use at an early age could help in preventing the initiation of eczema. However, several variables, such as the use of antibiotics, prenatal and postnatal diet, mode of delivery, and surrounding allergenic environment in the home, could impact the early-life colonization of probiotic strains. Nevertheless, the clinical administration of probiotics may become more widespread if the remaining questions are answered with strong evidence: what type of probiotic strain should be used? What dosage and time of administration should be used? At what time of life is the use of probiotics more efficacious? And most importantly, should the use of probiotics be personalized? Current analysis of the role of probiotics in the prevention of AD reveals that a positive effect may be related to the type of probiotic strain used, the method of administration, onset time, as well as the dose size and duration of treatment. However, these uncertainties need to be further clarified before corroborating the preventive impact of probiotics in the prevention and/ or treatment of AD.

Pigmentary disorders

↓

Basics (imp. جدا مهم)

- Color of Skin: caused by 4 factors:
  1. Hb —< oxyHb → red color; deoxyHb → Blue "
  2. Melanin → Brown
  3. Carotenoids: obtained from plant diet —< Orange, Carrots.

Melanocytes مهم

- Dendritic, Pigment synthesizing cell that derived from ! Neural crest & rests bet. KCs at BMZ.
- Embryology: Melanoblast (at Neural Crest) —differ. to→ Melanocytes
  → Migrate to:
  - Skin: Epid., dermis & H. Follicles.
  - Inner ear
  - Eye
  - Meninges
- Important Numbers: (أرقام مهمة)
  - development at 8 ws IU.
  - Earliest signs of Melanization: 10 ws IU
  - No: 2 x 10^9 (أكثر عدد —< Face, Genitalia)
  - No ↓↓ by 8% / 10 ys.
  - MCs : KCs ratio = 1:9 (1:4 – 1:10)
  - Each MC supplies Melanosomes to 36 KCs by process of Apocopation (Apical part of ! cell is released together with the secretory product) [Cytophagocytosis]

  أهم رقمين (1:9) & (36 KCs) → [the two items above]
- MIC Exam.: by H&E stain: They appear as a clear cells at basal cell layer ē deeply stained nucleus ---

(d.t Artefacts formed during Fixation of Specimen That's because MCs have — ⟨ desmosomes & Tonofilaments ⟩).

. DD from Clear spaces of KCs :?? They Show — ⟨ (cl. cell junction
Layer of cyto-
plasm peripheral
To the Halo.

. Special Stains: (مهم جداً)

(1) Fontan-Masson (MCs ع ... ...)

(2) DopA oxidase react.

(3) Immunohistochemical (Markers) —⟨ S 100 / Mart- 1 / HMB 45

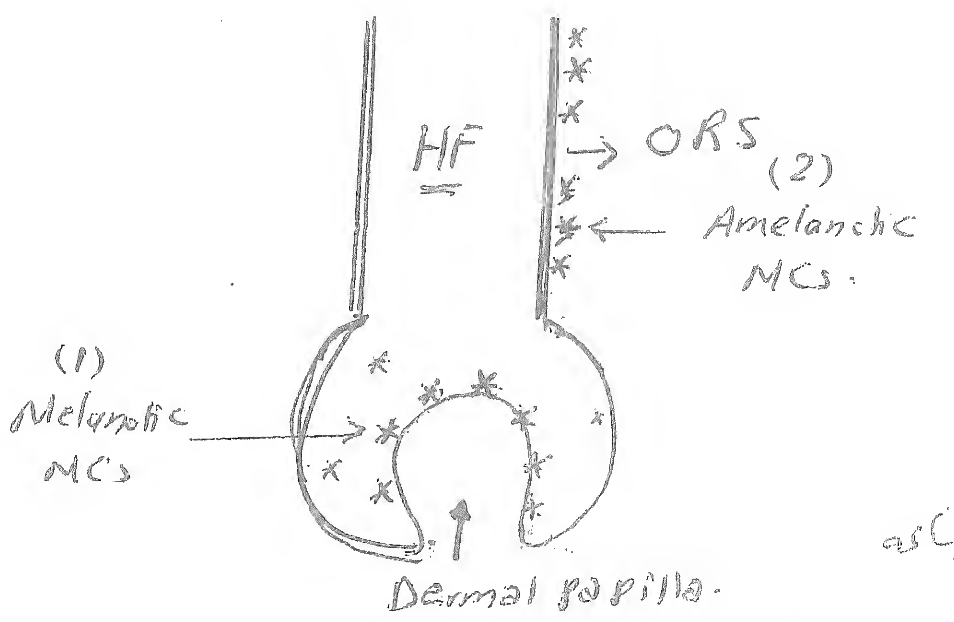
. NB DopA oxidase React. (...)

. Most specific Method

. depends on presence of Dopa oxidase (Tyrosinase) enz. inside MCs → so DopA + Skin Biopsy —Tyrosinase→ Melanin products (Brown-Black deposits).

(انواع الـ MCs في الجلد) Skin Melanocyte Populations (مهم جداً)

• Epidermal MCs
... ...
(Basal bet KCs)



• Hair-follicle MCs

Melanotic MCs (DOPA +ve)
↓
. interspersed bet. Matrical Cells of HF bulb .. Immediately Capping The dermal papillae (...)
. وظيفتها : امداد الشعر باللون ... Anagen

Amelanotic MCs (DopA − ve)
. Reservior MCs at ORS of HFs.
. under NL Skin Conditions → inactive
. under stress (injury, UVL) → prolif. & migrate to epid. Surface → Perifollicular pigmentation (Seen on Vitiligo Treated by UVB)

. Q1 what the difference bet. Melanotic & Amelanotic MCS of HFs ??
. Q2 difference bet. —⟨ epid. MCs & → ... ... / Melanotic MCs of HF → ... ... (Anagen)

NB Racial Differences in Skin Color is not Caused by differences of MCs Number (both dark & light skinned show KC : MCs = 9:1)

But This difference is d.t.

(1). Melanosome difference in — No / size / distributn

(2). Type of Melanin — Eumelanin (Brown-black) / pheomelanin (Red/white)

In Light Skin

Melanosomes — fewer / smaller / packaged by memb bound complexes

In dark Skin people

Melanosomes — Much / larger / Singly dispers...

Function of Melanocytes

(1) Melanin product —
- Color of Skin
- has Umbrella like actn over KCs Nucleus → protect them from UVL & so skin Cancer (so lighter skin people أكثر عرضة لسرطانات الجلد)
- Antioxidant → ↓ UVL effect on skin.

(2) MCs: Secrete Cytokines & express cell surface Ag ∴ suggest their active role in inflammatn.

Disadvantage of Melanin

① يمتص كمية أكبر من أشعة الشمس وبالتالي ينبعث منها ٣٠٪ أكثر من الحرارة داخل البشرة فيزيد درجة حرارة الجسم

② يمنع تكوين VitD ← فيسبب مرض الكساح منتشر في الأطفال السمر أكثر

•• Melanosomes in Different Colors

Light Skin	Dark Skin
. Stage II Melanosomes	. Stage III & IV
. Size < 0.5 μ	. > 0.5 μ
. No/MC < 20	> 20
. distribute: groups	. dispersed (single)
. Degradation: Fast	. Slow

Pathway of epidermal melanin pigmentation

(10 Steps)

1. Migrate of Melanoblasts ← نقص تكون → . Piebaldism . Waardenburg Synd.
↓
2. Differenthate into MCs
↓
3. Mitosis of MCs ← تثبيط → Vitiligo
↓
4. Synthesis of TYR ← ↓ → Albinism
enz.
↓
5, 6, 7. Synthesis of Melanosome → Chediak Higashi, Ash leaf of TSC.
↓
8. Melanosome Melanization → Albinism, PVC, IGH
↓
9. Melanosome Transfer
↓
10. Melanosome ← تراكم → . Chediak H. . Nevus depigment. . PVC . Pit. Alba.

• Melanin Synthesis

. phenylalanine aa
↓ pha Hydroxylase ← نقص إنزيم (phenyl ketonuria) (PKU)
Tryosine
Tyrosinase enz. ← DoPA → DoPA Quinone
. Pheomelanin
Eumelanin

. Eumelanin

. Ellipsoid melanosomes
. dark (brown-black)

• Pheomelanin

- Spherical
. Contain Cysteine.
. Light (Yellow or red)

(Basic) للبشرة فقط

Types of Skin Color = NL Pigment

1. Constitutive : Genetically determined
2. Facultative (Inducible) ← UVR, Hormones

- Caucasoids → white
- Mongaloid → Oriental
- Negroid → Black
- Australoid → Aboriginal

Control & Regulation of Skin Pigment

(1) Genetic factors (Constitutive)

(2) UVL : ↑ MCs, ↑ Melanosomes, ↑ Tyr. enz activity

(3) Immediate Pigment darkening (IPD) & delayed Tanning (see Light & Skin).

(4) Endocrinal : α-MSH, ACTH, Estrogen.

(5) Biochemical Factors : IL1α & β, IL6 & TGFβ

Enzymes & proteins involved in Melanogenesis.

- Tyrosinase enz.
- Tyrosinase Related protein (TRP1 & 2)
- Melanocortin Receptors (MCR1)
- MITF = Microophthalmia associated Transcription Factor
  ((if Mutate)) → (Waardenburg & Tietz Synd.)

Stages of Melanosomes Development (4)

- Stage I → Spherical No Melanin
- Stage II → Oval, great activity of Tyrosinase.
- Stage III : as stage II + moderate deposite of Melanin.
- Stage IV : oval, little activity of Tyr., Much Melanin.